ID 9541483

DATE	TIME	HR	ABPS	ABPD	ABPM	PAPS	PAPD	PAPM	CVP	VPB	TEMP	CO	PAWP	HT	WT	CI	SV	SI	SVR	SVRI	PVR	PVRI	LCW	LCWI	LVSW	LVSWI	RCW	RCWI	RVSW	RVSWI	BSA
14-may-91	1155	105	113	48	153					0																					
	1156	106	102	61	72	19	14	16		1																					
	1157	105	104	57	70	20	15	18		1																					
	1158	106	99	57	69	19	13	18		0																					
	1159																														
	1200																														
	1201																														
	1202	101	102	57	68	20	11	15		1																					
	1203	101	109	59	71	20	11	15		0																					
	1204	99	119	61	75	23	12	16		0																					
	1205	100	134	66	82	23	10	16		0																					
	1206	101	133	66	127	23	10	16		0																					
	1207																														
	1208																														
	1209																														
	1210	103	113	61	75	21	10	16		0																					
	1211	105	104	59	73	22	11	16		2																					
	1212	109	113	66	78	21	11	16		1																					
	1213	107	119	68	80	20	12	16		0																					
	1214	106	114	65	77	20	11	16		1																					
	1215	106	117	65	78	20	13	17		1																					
	1216	103	120	67	79	21	10	15		0																					
	1217	102	122	63	78	21	9	14		0																					
	1218	102	118	65	78	22	9	15		0																					
	1219	103	115	63	76	21	9	14		0																					
	1220	103	114	62	75	21	9	14		0																					
	1221	102	112	61	74	21	9	14		0	35 3																				
	1222	103	114	61	74	21	9	14		0	35 4																				
	1223	103	113	62	74	21	9	14		0	35 4																				
	1224	104	111	61	73	20	9	14	13	0	35 3	5 36																			
	1225	103	111	61	73	19	10	14	13	0	35 4	5 36	12				52		895		30		5 3		51 6		1 02		9 9		
	1226	102	110	61	73	19	10	14	13	0	35 4	5 36	12	175	84 5	2 67	52 5	26 1	895	1799	30	60	5 3	2 6	52 1	25 9	1 02	0 51	10	5	2 01
	1227	101	109	60	72	19	9	14		1	35 4																				
	1228	101	106	61	72	18	11	14		0	35 4																				
	1229	101	108	60	72	19	10	14		2	35 4																				
	1230	101	106	59	70	18	10	14		5	35 4																				
	1231	102	107	60	71	19	11	15		1	35 4																				
	1232	103	107	60	72	18	11	14		0	35 4																				
	1233	102	106	60	71	18	11	14		0	35 4																				
	1234	102	108	61	72	18	11	15		0	35 4																				
	1235	102	107	61	72	18	11	14		0	35 4																				
	1236	102	108	60	72	18	10	14		0	35 4																				
	1237	102	106	59	71	19	9	13		0	35 4																				
	1238	102	107	60	71	19	9	14		0	35 4																				
	1239	101	108	61	72	19	9	14		0	35 4																				
	1240	101	108	60	72	19	9	14		0	35 5																				
	1241	101	108	60	72	19	10	14		0	35 5																				
	1242	101	108	61	72	19	10	14		0	35 5																				
	1243	101	109	61	73	19	10	14		0	35 5																				
	1244	101	106	61	72	18	10	14		0	35 5																				
	1245	101	109	62	73	18	10	14		0	35 5																				
	1246	101	109	61	72	19	10	14		0	35 5																				
	1247	101	107	61	72	18	10	14		0	35 5																				
	1248	101	108	61	72	18	10	14		0	35 5																				
	1249	100	107	60	72	18	10	14		0	35 5																				
	1250	100	107	60	72	18	10	14		0	35 5																				
	1251	100	106	60	71	18	10	14		0	35 5																				
	1252	100	106	58	71	18	11	14		1	35 5																				
	1253	99	107	59	71	18	11	14		1	35 5																				
	1254	99	106	59	70	18	11	14		0	35 5																				
	1255	99	105	59	70	18	11	14		0	35 5																				
	1256	98	107	60	71	18	11	14		0	35 5																				
	1257	101	108	60	72	18	12	15		0	35 5																				
	1258	99	108	61	72	18	11	14		0	35 5																				
	1259	98	109	60	73	18	11	14		3	35 5																				
	1300																														
	1301																														
	1302																														
	1303	97	112	60	73	18	11	14		0	35 5																				
	1304	97	113	61	72	18	11	14		0	35 5																				
	1305	97	112	60	72	18	11	14		1	35 5																				
	1306	97	114	60	73	18	11	14		0	35 5																				
	1307	96	115	61	74	19	11	14		0	35 5																				

6.3 Expert Critiques

Expert critiques were the documented results of reviewing a historical CVICU case from the knowledge acquisition (KA) session. The critiques contained comments from the expert physician regarding the consistency of therapies instituted, preferred alternatives and recommendations on interventions not considered by the staff. Expert critiques from the 13 historical learning cases were used to formalize the expertise; those from the other 13 test cases were used to validate the performance of the prototype. The process of the KA session and an excerpt of the critiques from the historical case illustrated in the earlier sections of this chapter are presented below.

The KA Session

A typical KA session would begin with the expert physician examining the ward and pre-operative data, i.e. laboratory results, blood gases, cath lab data and surgical procedure. Based on this information, an initial impression was formed as to the pre-operative state of the patient.

The intra-operative and immediate post-operative data, e.g. MAP, CVP and/or PAWP at the time provided further information about the hemodynamic state. The Doctor's Order sheet included details of the post-operative ventilatory and hemodynamic management instructions for the patient. The expert physician either accepted or redefined the therapeutic target ranges for HR, MAP, CI, CVP, PAD and PAWP set earlier by the staff.

Once the therapeutic target ranges were determined, the expert would review the minute-by-minute hemodynamic profile printouts, correlating the hemodynamics with the target ranges, the other clinical data present the therapies instituted at the corresponding time point.

The expert would offer comments on his interpretations of the patient's condition and propose diagnostic and therapeutic interventions that he felt appropriate under the circumstance. Then he would review the therapies instituted, critiquing on their appropriateness and suggesting preferable treatments where appropriate. While discussing certain clinical conditions and the use of therapeutic interventions, the expert would elaborate on the underlying cardiovascular physiology and on the rationale of alternative management strategies. The anticipated hemodynamic response from the therapeutic agents used, based on the expert's experience, would also be discussed.

The review would continue until the end of the case when the patient was discharged from the unit. The expert would then provide a critique summary generalizing his observations, critiques and recommendations. He would also indicate clinical quality improvement opportunities that could have been exploited on the basis of the historical data. Each session was tape-recorded and transcribed for reference purposes.

Excerpt from a Knowledge Acquisition Session

(Based on data presented in the earlier sections of this chapter)
Case critique done on March 14, 1992

1155 May 14, 91 – hemodynamic parameters on admission to CVICU. Sinus tachycardia present 105. MAP 153, obviously an error.

1156 – tachycardia. PAD 16 normal. So aside from sinus tachycardia, normal. No CO done.

On admission to ICU, ventilator setting set to IMV say 8, PEEP 5, FiO2 70%, saturation at bedside 98%. Part of standard protocols, did not appear to have any aberrancy.

At 1130, ABG done, PO2 316, PCO2 42 and H 47, saturation 99%, base excess -4. Mild metabolic acidosis. Serum bicarb at 22 confirming the clinical impression. HCT was 30. For this amount of ventilation, these gases were appropriate, except for mild acidosis observation. Would not have treated but observe the patient for one hour, and repeat the gas.

Concurrently, CO indices were done within a short time at 1225, about an hour after first gas. Revealed CI of 2.6, adequate, confirmed no need to treat aberrant acidosis. Rest of cardiac profile not remarkable.

Patient appears to be stable at this time, dopamine and nitro running, may have optimized the hemodynamic profile. Running at 4.6 and 0.9 respectively, considered mild infusion rates, under these circumstances hemodynamic profile was adequate under minimal support. Drips on back of anesthetic record to summarize all drips. Assume at 1200, under conditions of dopamine and nitro infusion that we have adequate hemodynamic profile.

Patient also given oral NG, but don't know the detail. Plain is a drive to provide background flush to avoid a highly concentrated drugs producing a roller-coaster effect. Running at 10 ml per hour with 2/3 and 1/3, also KCl, likely part of same drive mechanism through a manifold and oral med NG noted.

At 1205, albumin 5% 250ml given. Hemodynamic profile PAD at 10, no CVP, suggest an appropriate maneuver to give a bit of volume. From a cost perspective, $100 a shot for albumin, far better off to give std ringer's lactate at $1.25 a bag. An expensive maneuver that don't believe to be warranted. There was sign of relative hypovolemia with PAD at 10. Based on these numbers, it is an empirical maneuver that would have been easily assessed over the next 15 minutes to see what indeed happens to the filling pressure. If we track down next 15 minutes after albumin was given, we can see that filling pressure indeed rose by observing the PAD, no CVP. This was also the point where the MAP was stabilized at about 80 plus or minus 2. So it was a correct maneuver.

At 1205, when albumin given, NaHCO3 also given, based on -4 base excess. Actually done at 1130, a bit of a lag period. Let's assume it came back in half-an-hour. I am not sure I would have treated that, give the patient a chance to equilibrate.

Hemodynamic observations to 1300, a number of therapeutic maneuvers, dopamine and nitro at same levels. KCl given, presumably based on K from lab, drawn at 1210 with 4.0. About one hour ago. Urine 920 ml was a tremendous amount over a two-hour period. In the presence of oliguria, would have been more careful and observe K level closer in terms of lab value. In this case, there was a tremendous amount of urine output, and the K value was only 4, predictably knowing it to decrease, so maneuver was proper. Bring it to 5. In case of arrhythmia even to 5.5. But in this case, order for K was bolus to 5.

CHAPTER 7

THE PROTOTYPE

The conceptual and technical design of the knowledge-based, decision-support system prototype is described in this chapter. The description consists of an overview, the knowledge base, the reasoning and control processes, and the technical design of the system. The prototype design was based on knowledge extracted from textbooks, the CVICU nurses, a pharmacist, the two expert physicians and the 13 critiqued historical CVICU learning cases.

7.1 System Overview

An overview of the cardiovascular model, clinical variables and conceptual decision framework for managing hypovolemic hypotension used in the study is outlined in this section.

7.1.1 Model and Variables

The framework adopted a cardiovascular model similar to that proposed by Shoemaker (1989), which expressed cardiovascular performance in four dimensions – pressure, volume, flow and function. Only physiologic parameters routinely measured and evaluated in CVICU were represented in the model. Although data from over 70 clinical variables were collected for each CVICU case, the knowledge acquisition revealed the variables relevant to hypovolemic hypotension were:

- ABPS, ABPD, PAPS, PAPM, MAP, PVRI, SVRI for pressure
- CI and HR for flow
- CVP, PAWP, PAD and MAP for volume
- Blood gases, serum K, Ca, ionized Ca, Mg and total CO_2 as proxy measures for function
- Urine, CT loss, weight gain for intake/output balance, which reflects volume status
- CT loss, HB and HCT for blood loss, which reflects volume status
- PT, PTT, PLT for coagulopathies associated with bleeding
- OSM, Na for guiding fluid replacement
- Temperature for hypothermia and vasoconstriction
- All inotropic and vasoactive therapies
- All fluid therapies
- All anti-coagulopathy therapies
- All electrolyte-replacement therapies
- Other medications including analgesics, diuretics and anti-arrhythmic agents

Only the relevant clinical variables were included in the design of the decision framework. Both magnitude and trend of the hemodynamic parameters are used to assess the status of cardiovascular performance. Depending on their values at a given time, the respective flow, pressure, volume and function dimensions can be instantiated to reflect the overall cardiovascular performance status. For example, in the situation where CVP, PAWP, CI and MAP are reduced, so are the corresponding volume, flow and resistance, leading to low cardiovascular performance, i.e. hypovolemic hypotension. Similarly, low levels of serum Ca, K and/or Mg ions or severe acidosis can lead to compromised function, resulting in myocardial ischemia and dysfunction.

7.1.2 Conceptual Framework

A conceptual decision framework was developed to provide the basis for therapeutic management of hypovolemic hypotension. The major components of this framework are its knowledge base and reasoning processes. The structure and flow of the decision framework are shown in Figure 18. Rectangles indicate processes; arrows indicate flow. The processing is cyclical until there is no more patient data. The processes are summarized below.

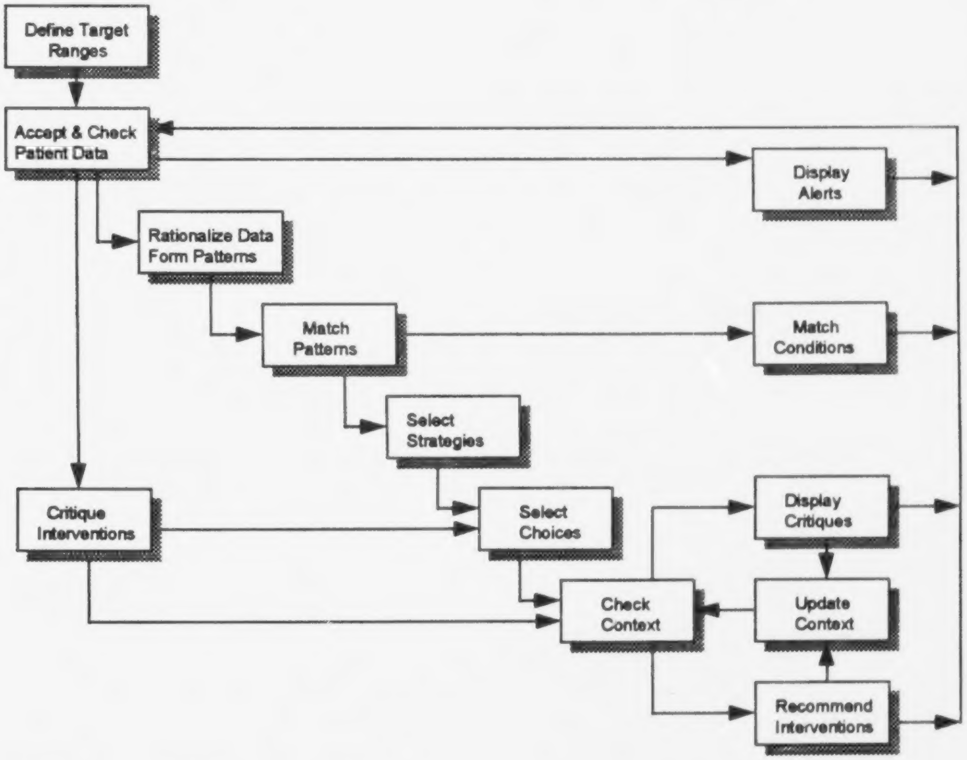

Define Target Ranges
Accept & Check Patient Data
Display Alerts
Rationalize Data Form Patterns
Match Patterns
Match Conditions
Select Strategies
Critique Interventions
Select Choices
Display Critiques
Check Context
Update Context
Recommend Interventions

Figure 18. The conceptual decision framework.

Define Target Ranges

At the beginning of the analysis, the target ranges for HR, MAP, CI, PAD, PAWP and CVP of the patient are customized as defined by the expert physician. The ranges were defined based on the cath lab, pre-op, intra-op and immediate post-op data. The standard reference range is used if no target range was defined for the hemodynamic parameters. Standard reference ranges are also used as target ranges for the other physiologic parameters, such as the laboratory data.

Accept & Check Patient Data

The processing cycle starts by accepting the next available set of hemodynamic data on the patient. Depending on timing, the set may also include laboratory and blood gas data, ventilation data, fluid intake/output and actual interventions. The difference in timing is because the hemodynamics were available on a minute-to-minute basis, while the others were less frequent. Cross-validation is done on selected hemodynamic data to ensure their accuracy.

Rationalize Data and Form Patterns

Selected parameters are rationalized into 8-valued numeric codes based on target and standard reference ranges. The codes are combined to form physiologic patterns. Six individual patterns are constructed:

- Hemodynamic status
- Hemodynamic trend
- Laboratory
- Blood gases
- Fluid i/o
- Coagulation

A group-pattern is also created by combining hemodynamic status and trend as the hemodynamic-status-trend pattern.

Match Patterns

The physiologic patterns constructed are matched to known patterns, which were created from the 13 learning cases and stored in the knowledge base for pattern-matching.

Match Conditions

Each known pattern was matched to one or more known clinical conditions when created, such as moderate hypotension. Known conditions were created from the 13 learning cases and stored in the knowledge base. By matching the constructed patterns to the known patterns in the knowledge base, the patient's condition can be determined. The matched conditions are displayed.

Select Strategies

The known patterns for hemodynamic status, hemodynamic trend, laboratory, blood gases, fluid I/O and hemodynamic-status-trend were matched to one or more intervention strategies when created, such as reduce-volume-deficit. By matching the constructed patterns to the known patterns, the intervention strategies can be determined. There are two types of strategies, diagnostic and therapeutic. Time lags are built into strategies, causing a delay of 0 to 10 minutes before the strategies are invoked. Patterns for less severe conditions are assigned pending strategies with a positive time delay. An algorithm was designed to decrement the time delay during each processing cycle. Strategies with 0 minute time delay are invoked, or selected for action.

Select Choices

Once a strategy has been invoked, the next step is to select from a set of action alternatives, called intervention choices, which may be a diagnostic test, a replacement for an electrolyte, an agent for bleeding or a fluid (crystalloid or colloid). For bleeding and fluid replacement, the agent selected depends on certain laboratory parameters and is guided by the protocols. With fluids, the amount needed is further determined through the net-difference scoring and ranking algorithms. The algorithms compute the expected hemodynamic responses for candidate agents/dosages and choose the one that brings the hemodynamics closest to or within the target ranges. The dosage for inotropes and vasoactive agents is also selected by net-difference scoring and ranking, but the selection is invoked through critiquing instead (described next).

Critique Interventions

At present, vasoactive and inotropic therapies instituted are critiqued only. Three types of critique are used on inotropes and vasoactive agents:

- If the patient is on vasoactive therapy, the net-difference scoring and ranking algorithms would be invoked during each cycle to critique if a change in dosage is needed.
- Any time there is a change in the actual inotropic or vasoactive therapy, the algorithms are also invoked to critique if the change is appropriate. An alternative dosage is proposed if it had better hemodynamic responses than the dosage being changed.
- Weaning is proposed for inotropes and vasoactive agents that met the weaning criteria.

Critiquing is also used in two other circumstances:

- For each therapy instituted, reverse protocols are applied to see if the intervention met the criteria justifying its use. This applies to all therapies except the inotropes and vasoactive agents.
- The target ranges for CVP, MAP, PAD and PAWP are checked to see if they need to be redefined due to any change in patient's condition.

Check Context

Once an intervention choice has been selected, the patient's current context is examined. If the intervention had already been instituted or proposed by the system earlier, the recommendation is amended accordingly. The expected impact of the interventions is interpreted from the net-difference scores. For proposed therapeutic agents, the system also computes the expected percentage of improvement in the net-difference score if the agent were instituted.

Display Alerts

Alerts are displayed on questionable data, such as data that failed the cross-validation checks.

Display critiques

Critiques are displayed on all therapeutic interventions instituted, either concurring with the actions taken or proposing alternate intervention choices to be made.

Recommend Interventions

Recommendations are displayed on proposed intervention choices, which may be diagnostic tests to be performed or therapeutic agents for fluid therapy. The expected percentage of improvement in the net-difference score and overall impact on the patient's condition are also displayed.

Update Context

At the end of every processing cycle, the patient's context is updated to reflect the clinical data accepted, therapeutic interventions instituted, as well as any proposed alerts, critiques and recommendations. For any therapy instituted that affected the hemodynamics, an assessment is made to determine the actual drug-dosage response, which is incorporated into the general drug-dosage response tables to render them patient-specific over time.

7.2 Knowledge Base

The knowledge elicited from the expert sources – reference and target ranges, physiologic patterns, clinical conditions, intervention strategies, therapeutic agents and their drug-dosage responses, and therapeutic and reverse protocols – was formalized as the basis of the decision framework. The structure and usage of the resulting knowledge base are described in this section.

7.2.1 Reference and Target Ranges

Standard reference ranges are provided for all physiologic parameters used in the system. Four pairs of numeric low-high thresholds were defined for each parameter, as warning, alert, critical and physiologic limit, respectively. For instance, the reference ranges for ABPD (in mmHg) were set to thresholds of 60/90 for warning low/high, 50/100 for alert low/high, 40/110 for critical low/high and 20/140 for physiologic low/high limit. The two physiologic limit thresholds are used for data validation, any data outside their range being rejected. The other thresholds are for data rationalization and pattern construction, any values between the warning thresholds being regarded as within target.

Hemodynamic management involves therapeutically maintaining the hemodynamic parameters within desirable, or target, ranges. The target ranges of key parameters are often customized relative to each patient's underlying condition, prescribed medications, and pre-op, intra-op and post-op hemodynamic status. The customization can also be dynamic, set initially upon admission to the CVICU and progressively adjusted during the case, depending on the patient's condition.

Customization consists of resetting the warning thresholds of the standard reference ranges, i.e. redefining the desirable range that is the target of management. Whenever these inner thresholds are adjusted, corresponding adjustment is made automatically to the alert and critical thresholds; this is done by prorating each side of the target relative to the respective physiologic limit, which is fixed. The modified set of thresholds is called the customized reference ranges for the current patient. Current customization practice applies to only six key hemodynamic parameters (HR, CVP, MAP, CI, PAD, PAWP); no cause was seen for customizing others – the standard ranges being used without alteration.

Generally, the target ranges set by the physician are oriented to the long-term characteristics of the patient. For instance, if a patient's ejection fraction was less than 40%, and the filling pressures (CVP and PAWP) at intra-op and immediate post-op were greater than 10, then a stiff ventricle would be expected. The target ranges for CVP, PAWP and PAD would be set higher, e.g. 12-18 mmHg, relative to those with normal ventricles. However, the target ranges can also be adjusted to meet short-term objectives. For example, in an active bleeding situation immediately post-op, MAP may be set at lower than ultimately desired to minimize blood loss. Once bleeding subsided, the long-term target for MAP can then be applied.

Because of the inherent complexity, a decision was made to let the expert physician customize the initial target ranges for both the learning and test cases. A range redefinition heuristic was provided in the system to redefine the target range if certain predefined criteria were met (see section 7.3.9).

7.2.2 Physiologic Patterns

The role of physiologic patterns is threefold. First, they represent the overall status of the patient at a given time. Second, the patterns can be matched to one or more clinical conditions, providing a meaningful interpretation of the patient's status. Third, each pattern is sufficiently specific to be matched with one or more intervention strategies. In the study, known patterns were constructed from the learning cases and matched to specific conditions and intervention strategies. The known patterns are stored as part of the knowledge base and used for matching against the constructed patterns of a patient from the test case.

The physiologic patterns are based on parameters that can best summarize the patient's conditions. Six individual patterns are used: hemodynamic status; hemodynamic trend; laboratory; blood gases; fluid i/o; coagulation. The two hemodynamic patterns are also combined as the hemodynamic-status-trend pattern.

Fluid i/o patterns are based on six parameters to form a 6-digit number. Other individual patterns are based on five parameters, hence of 5 digits. Each parameter is compared against its customized/standard reference ranges in forming the pattern. Since each of the parameters has three thresholds below target, three above, giving seven levels, allowing for unknown makes 8 values for each of the positions. A coding scheme of 0 to 7 is used: 0 for unknown; 1 for critical low; 2 for alert low; 3 for warning low; 4 for target; 5 for warning high; 6 for alert high; 7 for critical high. Feasible permutations of the 5-digit octal number are 32,768; but only 466 known patterns occurred in the 13 learning cases.

The data rationalization and pattern construction technique is illustrated with the hemodynamic status pattern. The five hemodynamic parameters considered representative of cardiovascular performance are HR, MAP, CI, PAD and CVP. For data smoothing, the median value over five minutes was used as the real-time resolution of the hemodynamic data actually available every minute (described in 7.3.1). Examples of the rationalization/construction are shown in Table 4.

(a) 3=Critical, 2=Alert, 1=Warning, 0=No aberration								(b) Examples						
ALARM	HR	MAP	CI	PAD	CVP	CODE	INTERPRETATION	CASE	HR	MAP	CI	PAD	CVP	CODE
-3	< 40	50	1.5	2	2	1	Critical low	1	84	67	2.1	16	14	43344
-2	< 50	60	1.8	4	4	2	Alert low	2	108	64	2.7	16	14	43444
-1	< 60	70	2.2	6	6	3	Warning low	3	90	86	2	15	12	44344
0						4	Acceptable/Target	4	89	85	1.9	17	13	44354
1	>110	100	3.5	16	16	5	Warning high	5	126	80	3	21	15	64474
2	>120	110	3.8	18	18	6	Alert high	6	88	72	1.9	20	14	43464
3	>130	120	4.2	20	20	7	Critical high	7	101	94	2.7	26	20	44476
N/A	.	.	.	.	.	0	Not available							

Table 4. Examples of hemodynamic status patterns constructed from the target ranges defined for a patient. The 5-digit code represents HR, MAP, CI, PAD and CVP, respectively, from left to right. (a) shows the thresholds used to translate the hemodynamic value into a code of 0 to 7; (b) shows 7 sets of patterns with the translated codes. Note Acceptable is same as Target.

A similar approach was also adopted to determine the trend of the five hemodynamic parameters. First, the coefficients of the linear regression model, Y = a + bX (Harnett 1982), were computed for each of the five parameters over the most recent 15-minute interval. The sign of the slope indicated the direction of the trend (increasing or decreasing). Then the rate of change over the interval was calculated as a percentage. Arbitrary thresholds were used to rationalize the percentage change: a 5 to 15% change was rationalized as mild; 16 to 30% as moderate; >30% as marked. By applying these thresholds, and allowing for no change and unknown, an 8-valued code was again obtained for each parameter. Illustrations of the trend construction are shown in Table 5.

When an explicit trend was registered, the hemodynamic trend pattern would be appended to the status pattern to give a hemodynamic status-trend pattern, e.g. 53030-43030.

(a) Hemodynamic Trend Patterns							(b) Example						
HR	MAP	CI	PAD	CVP	CODE	INTERPRETATION	Time	HR	MAP	CI	PAD	CVP	Pattern
< -30	-30	-30	-30	-30	1	Markedly decreasing							
< -15	-15	-15	-15	-15	2	Moderately decreasing	5	102	78	.	.	8	
< -5	-5	-5	-5	-5	3	Mildly decreasing	10	98	82	.	.	10	
					4	No change	15	84	93	.	.	10	
> 5	5	5	5	5	5	Mildly increasing	slope	-0.2	0.2	.	.	0	
> 15	15	15	15	15	6	Moderately increasing	%	17	20			0	
> 30	30	30	30	30	7	Markedly increasing	Pattern	2	5	0	0	0	25000
.	.	.	.	.	0	Not available							

Table 5. Illustrations of three types of hemodynamic trends are shown for MAP based on its values over the most recent 15 minutes. **(a)** the interpretations based on the rate of change in % and direction for each parameter; **(b)** Examples of the trends for three of the five parameters and how they form the trend pattern.

Patterns for coagulation, fluid i/o, blood gases and laboratory can be constructed using the same technique. The physiologic parameters used are:

- HCT, HB, PT, PTT and PLT for coagulation
- Urine, Urine-4-hours, CT, CT-3-hours, i/o-balance and %WT change for fluid i/o
- pO_2, pCO_2, H, SaO_2, Base for blood gases
- K, Total CO_2, ionized Ca, Ca and Mg for laboratory

Examples of these patterns are shown in Tables 6 (a) to (d). Of the patterns described, only hemodynamic status, hemodynamic trend, hemodynamic-status-trend, laboratory and fluid i/o patterns were matched to specific intervention strategies. The remaining patterns were strictly used for matching clinical conditions.

(a) Coagulation Patterns:

(a) 3=Critical, 2=Alert, 1=Warning, 0=No aberration

ALARM	HCT	HB	PT	PTT	PLT	CODE	INTERPRETATION
-3	< 24	8	0.4	20	40	1	Critical low
-2	< 26	10	0.6	22	60	2	Alert low
-1	< 28	12	0.8	25	80	3	Warning low
0						4	Acceptable
1	> 48	15	1.0	40	340	5	Warning high
2	> 50	17	1.2	46	360	6	Alert high
3	> 52	20	1.6	50	400	7	Critical high
N/A	.	.	.	.	.	0	Not available

(b) Examples

CASE	HCT	HB	PT	PTT	PLT	CODE
1	27	14	1.5	36	223	34644
2	32		1.5	34	175	40644
3	30	13	1.4	32		44640
4	27					30000
5	25	11	1.5	23	220	23634
6		14	1.4	34	125	4644
7				27	120	44

(b) Fluid i/o Patterns:

(a) 3=Critical, 2=Alert, 1=Warning, 0=No aberration

ALARM	UR	UR4	CT	CT3	IO	WT	CODE	INTERPRET
-3	< 0.1	0.1	0	0	-4	-20	1	Critical low
-2	< 0.3	0.3	0	0	-2	-10	2	Alert low
-1	< 0.5	0.5	0	0	-1	0	3	Warning low
0							4	Acceptable
1	> 30	30	3.0	3.0	10	10	5	Warning high
2	> 60	60	5.0	5.0	20	20	6	Alert high
3	> 90	90	7.0	7.0	50	30	7	Critical high
N/A	.	.	.	.	.	.	0	Not available

(b) Examples

CASE	UR	UR4	CT	CT3	IO	WT	CODE
1	22	18		0	0	0	440444
2	1.2	1.1			0	0	440044
3	0.3	0.3		0	0	0	340444
4	0.4	0.3	1.0	2.0	0	0	334444
5	25	12	0	0	-2	-11	444423
6	12	13	0	0	-1	1	444434
7	1.5	2.0	0	0	0	12	444445

(c) Blood Gas Patterns:

(a) 3=Critical, 2=Alert, 1=Warning, 0=No aberration

ALARM	pO2	pCO2	H	SaO2	BASE	CODE	INTERPRET
-3		31	32	90	-6	1	Critical low
-2		33	35	94	-4	2	Alert low
-1		35	37	97	-2	3	Warning low
						4	Acceptable
1		42	42	100	2	5	Warning high
2		44	44	100	4	6	Alert high
3		47	46	100	6	7	Critical high
N/A						8	Not available

(b) Examples

CASE	pO2	pCO2	H	SaO2	BASE	CODE
1		42	47	99	-4	04743
2		32	35	99	1	02344
3		26	28	99	3	01145
4		27	32	99	-1	01244
5		27	34	98	-2	01244
6		27	35	99	-2	01344
7		31	35	99		02340

(d) Laboratory Patterns

(a) 3=Critical, 2=Alert, 1=Warning, 0=No aberration

ALARM	K	CO2	ionCa	Ca	Mg	CODE	INTERPRETATION
-3	3.0	17	0.80	1.60	0.4	1	Critical low
-2	3.5	20	1.05	1.80	0.6	2	Alert low
-1	5.0	23	1.20	2.00	0.8	3	Warning low
						4	Acceptable
1	5.2	31	1.34	2.65	1.05	5	Warning high
2	5.5	34	1.40	2.85	1.10	6	Alert high
3	5.8	37	1.45	3.05	1.15	7	Critical high

(b) Examples

CASE	K	CO2	ionCa	Ca	Mg	CODE
1	4.0	23.2	1.12	2.0	0.64	33343
2	4.0	18.5	1.31	2.4		32440
3	4.1	22.3	1.16	2.17		33340
4	4.6			2.55		30000
5				2.23	0.72	00043
6	4.6					30000
7	4.5	24.0	1.21	2.29		34440

Table 6. (a) coagulation patterns; (b) fluid i/o patterns; (c) blood gas patterns; (d) laboratory patterns.

7.2.3 Clinical Conditions

Each known pattern can be matched to one or more clinical conditions. On the other hand, many patterns are gradations of the same condition. For instance, hemodynamic status patterns 43344, 53444, 43454 and 63444 all indicate mild hypovolemia. Other examples of this type of pattern-matching are shown in Figure 19. In the study, 120 known conditions were identified from the 13 learning cases (with 466 patterns). The known conditions are of several types:

- Hemodynamic status conditions, e.g. mild, moderate and marked hypotension
- Hemodynamic trend conditions, e.g. mildly, moderately, markedly increasing MAP
- Abnormal coagulopathy conditions, e.g. prolonged PT-INR and/or PTT
- Abnormal electrolyte conditions, e.g. mild, moderate and marked hypokalemia
- Abnormal i/o conditions, e.g. mild, moderate and marked oliguria and bleeding
- Abnormal laboratory conditions, e.g. mildly, moderately and markedly reduced HB
- Abnormal blood gas conditions, e.g. metabolic acidosis

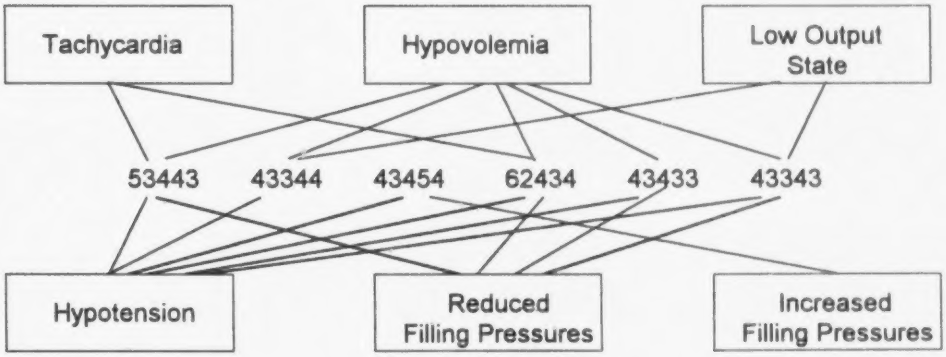

Tachycardia
Hypovolemia
Low Output State
53443
43344
43454
62434
43433
43343
Hypotension
Reduced Filling Pressures
Increased Filling Pressures

Figure 19. Examples of hemodynamic status patterns matched to clinical conditions.

7.2.4 Intervention Strategies

An intervention strategy represents a general approach to managing a clinical problem. For instance, a condition with decreased MAP and CVP, and increased HR suggests hypovolemic hypotension. The corresponding intervention strategy is to reduce this volume deficit. Also, a diagnostic test is usually conducted to confirm or rule out the suspected condition. An example is to perform the modified Trendelenburg test when hypovolemic hypotension is suspected. The two intervention strategies illustrated form a basic plan for managing hypovolemic hypotension.

A set of intervention strategy protocols was formalized through knowledge acquisition with the experts. The intervention strategies used in the study are listed in Table 7. Examples of the protocols are shown in Table 8. The complete set is in Appendix D.

Therapeutic ->	Continue to monitor
	Give bicarbonate
	Give calcium
	Give magnesium
	Give potassium
	Reduce volume deficit
	Stop active bleeding
Diagnostic ->	Check cardiac dysfunction
	Check cardiac output
	Check CVP/ART line for missing data
	Check dysrhythmia
	Check hyperdynamic state
	Check hypertension
	Check missing HR data
	Confirm CVP/ART data for fluctuations
	Modified-Trendelenburg-position

Table 7. Intervention strategies used in the study.

2.1	if	MAP = low
	and	(CVP or WP or PAD) = low
	and	(CT >= 3 ml/kg/hr and CT < 5 ml/kg/hr for 3 hours) or (CT >= 5 ml/kg/hr)
	then	
		condition = active bleeding, hypotension, absolute hypovolemia
		intervention-strategy = reduce-volume-deficit
		intervention-strategy = return-to-OR
2.3	if	MAP = low
	and	(CVP or WP or PAD) = low
	and	(HR = normal) or (HR = high and VPB < 5) or (HR = high and sinus-rhythm present)
	and	(CT >= 1 ml/kg/hr and < 3 ml/kg/hr for 3 hours)
	or	(CT >= 3 ml/kg/hr and < 5 ml/kg/hr)
	and	(URINE < 0.5 ml/kg/h) or (URINE >= 0.5 ml/kg/hr)
	and	(I/O-balance >= -1 litre) or (I/O-balance < -1 litre)
	then	
		condition = absolute-hypovolemia, hypotension, bleeding and/or oliguria
		intervention-strategy = check all catheter lines, cuff-pressures and rezeroing
		intervention-strategy = stop-active-bleeding
		intervention-strategy = reduce-volume-deficit
2.4	if	MAP = low
	and	(CVP or WP or PAD) = low
	and	(HR = normal) or (HR = high and VPB < 5) or (HR = high and sinus-rhythm present)
	and	CT < 1 ml/kg/hr
	and	(URINE < 0.5 ml/kg/h) or (URINE >= 0.5 ml/kg/hr)
	and	(I/O-balance >= -1 litre) or (I/O-balance < -1 litre)
	then	
		condition = absolute-hypovolemia, hypotension and/or oliguria
		intervention-strategy = check all catheter lines, cuff-pressures and rezeroing
		intervention-strategy = reduce-volume-deficit
4.1	if	MAP = low
	and	(CVP or WP or PAD) = high or normal
	and	HR = normal or high
	and	SVRI = low or normal
	and	PVRI = normal and CI = normal or high
	and	(K and Ca and pCO2 and CO2 and Base and H = normal)
	and	URINE >= 0.5 ml/kg/hour
	and	vasodilators = present
	then	
		condition = relative-hypovolemia, hypotension, normal cardiac function
		intervention-strategy = check all catheter lines, cuff-pressures and rezeroing
		intervention-strategy = reduce-vasodilator

Table 8. Examples of intervention strategy protocols. The numbering scheme for the protocols uniquely identifies each rule. The abbreviation WP is equivalent to PAWP.

A problem in applying the strategy protocols is that the institution of a strategy is also influenced by the severity of the conditions. For instance, in mildly hypotensive situations, the strategy is usually "wait-and-see", hoping that the condition is transient and self-correcting; this is widely practiced for mild aberrations. But the incorporation of condition severity into the protocols would increase their permutations, rendering the protocols difficult to maintain. Furthermore, the only difference between the protocols with varying severities is that of timing. For example, when CVP, MAP and PAD are markedly decreased, the institution of fluid therapy is immediate, whereas if the same parameters are mildly decreased, fluid therapy is instituted only if the condition persists for ten more minutes.

The use of physiologic patterns appeared ideal in avoiding redundant protocols. Specifically, formation of a pattern according to thresholds allowed the severity of the condition to be characterized and mapped to the same intervention strategies. For instance, hemodynamic status patterns 52333, 53002, 63003 and 71002 represent varying gradations of hypovolemic hypotension, which can all be mapped to "reduce-volume-deficit". Where one waits for an elapsed interval before instituting the therapy, strategies such as "reduce-volume-deficit-in-10-minutes" can be used. This would leave the strategy pending for 10 minutes before it is invoked. Alternatively, if the initiation of the intervention is immediate, "reduce-volume-deficit-now" can be used. A similar approach can be used with diagnostic interventions to rule out or confirm a condition, such as "check-line-in-10-minutes" and "check-arrhythmia-now". Examples of the final intervention strategy protocols in pseudo-rule form are shown in Table 9. A time delay of 0 to 10 minutes was built into most strategies. A time-delay algorithm was incorporated in the system to decrement positive time delays during each cycle. If the time delay is 0 minute, the pending strategy is selected, or invoked immediately. Exceptions are the electrolyte replacement strategies, which are invoked directly with no delay when matched from the patterns.

```
IF      Hemodynamic status pattern = 41050
THEN    Intervention-strategy = confirm-lines-now, check-cardiac-dysfunction-now
        Intervention-strategy = reduce-volume-deficit-in-5-minutes

IF      Hemodynamic status pattern = 42030
THEN    Intervention-strategy = confirm-lines-in-5-minutes
        Intervention-strategy = reduce-volume-deficit-in-5-minutes

IF      Hemodynamic status pattern = 43334
THEN    Intervention-strategy = confirm-lines-in-10-min, check-cardiac-dysfunction-in-10-minutes
        Intervention-strategy = reduce-volume-deficit-in-10-minutes
```

Table 9. Examples of intervention strategies in pseudo-rule form.

7.2.5 Intervention Choices

An intervention choice can be a diagnostic test or a therapeutic agent. The latter may be an inotrope, an vasoactive agent, a fluid, a target range redefinition, a treatment for active bleeding or electrolyte replacement. In the study, a set of therapeutic protocols was formalized to manage fluid replacement and bleeding. The protocols are invoked if "reduce-volume-deficit" or "stop-active-bleeding" was selected as the intervention strategy. The selection of the intervention choice, in this case an agent, from the protocols is contingent upon several factors. For bleeding, anti-coagulopathy agents such as protamine, cryoprecipitate, platelets and fresh-frozen plasma are chosen according to PT, PTT and PLT results. In fluid replacement, the type of crystalloid or colloid used depends on the levels of serum Na, OSM, HCT and HB. The amount of fluid required is computed using the net-difference scoring and ranking algorithms (see section 7.3.3). Examples of protocols used in fluid replacement and bleeding are shown in Table 10. The complete protocols are in section 10 of Appendix D.

10.4	if	intervention-strategy = reduce-volume-deficit
	and	(HCT within last 12 hours < 24) or (HB within last 12 hours < 8)
	then	intervention-choice = packed-cells
10.7	if	intervention-strategy = reduce-volume-deficit
	and	(OSM within last 6 hours >= 280) and (OSM within last 6 hours <= 300)
	and	weight-gain < 10% admission-weight
	and	(serum Na within last 6 hours >= 135) and (serum Na within last 6 hours <= 150)
	and	(URINE > 1 ml/kg/hour) or (URINE < 1 ml/kg/hour)
	and	(I/O-balance < -1 litre) or (I/O-balance > -1 litre)
	then	intervention-choice = ringers lactate
10.11	if	intervention-strategy = reduce-volume-deficit
	and	(OSM within last 6 hours >= 295) and (OSM within last 6 hours < 300)
	and	serum Na within last 6 hours < 150
	and	clinical-findings = edema or (weight-gain > 10% admission-weight)
	then	intervention-choice = 5% albumin
10.12	if	intervention-strategy = stop-active-bleeding
	and	PT-INR > 1.8
	then	intervention-choice = fresh-frozen-plasma
10.13	if	intervention-strategy = stop-active-bleeding
	and	PTT > 40
	then	intervention-choice = protamine 50 mg

Table 10. Examples of therapeutic protocols.

Critiquing rules were developed to determine the intervention choice when the patient is on vasoactive therapy, or there is a change in the actual inotropic or vasoactive therapy. If the patient is on vasoactive therapy, the net-difference scoring and ranking algorithms can be used to determine if dosage adjustment is needed. For a change in actual therapy, it may be the addition of a new agent, dosage adjustment for an existing agent or its discontinuation. The net-score and ranking algorithms can be used to determine if the change was appropriate. Alternative dosages up to two times the dosage of the agent being changed are included in the computation. The dosage with the lowest net-difference score becomes the intervention choice.

Rules were also developed to select an electrolyte-replacement therapy or a diagnostic test as the intervention choice when the corresponding intervention strategy was invoked. For electrolyte therapies, the choice is selected immediately with no time delay. For diagnostic tests, the same time delay technique is used. Weaning of patients from medication and target-range redefinition is based on predefined criteria and are described in sections 7.3.8 and 7.3.9, respectively.

7.2.6 Therapeutic Agents

Information compiled on therapeutic agents included pharmaceutical (drug class, route of administration, infusion interval, usual dosage, strength and unit), pharmacokinetic (onset delay, time to maximal effect, effect duration) and pharmacodynamic data (expected drug-dosage response).

The drug class distinguishes whether the agent is a colloid, crystalloid, positive inotrope, vasodilator, or miscellaneous (such as analgesic). The route of administration and infusion interval identify whether the agent is administered as continuous intravenous infusion or bolus and how long the infusion takes on average. The onset delay, maximal effect and effect duration indicate the time delay until the drug takes effect, the time it takes to reach maximal effect, and the interval for residual effect after its discontinuation, respectively. For instance, with 250 mL of 5% albumin, its drug class is colloid; it is usually infused as IV bolus over 15 to 30 minutes, with an onset delay of 10 to 15 minutes and reaching maximal effect within 30 minutes, with 1 to 2 hours of residual effect afterwards.

For simplicity, all colloids, crystalloids, inotropes and vasodilators were assumed to reach maximal effect within 15 minutes and would be assessed for their effectiveness at the end of the 15-minute period. Also assumed were the absence of side-effects, contraindications and interaction effects. A complete list of all of the agents used in the study is shown in Table 11. The drug-dosage response for each agent is discussed in the next section.

CATEGORY	NAME	CODE	UNIT	ROUTE
Crystalloids	ringers lactate	12210	mL	IVC
	normal-saline	12220	mL	IVC
	d5w	12250	mL	IVC
Colloids	albumin-5	12310	mL	IVC
	albumin-25	12320	mL	IVC
	autotransfusion	12390	mL	IVC
	fresh-frozen-plasma	12330	mL	IVC
	cryoprecipitate	12360	mL	IVC
	packed-cells	12340	mL	IVC
	platelets	12370	mL	IVC
IVs	amicar	13110	mg/hr	IVC
	bretylium	54110	mg/hr	IVC
	dobutamine	22210	mcg/kg/min	IVC
	dopamine	22310	mcg/kg/min	IVC
	epinephrine	22320	mcg/kg/min	IVC
	inocor	24110	mcg/kg/min	IVC
	cz-insulin	63110	mcg/hr	IVC
	isuprel	22110	mcg/min	IVC
	nipride	41110	mcg/kg/min	IVC
	nitroglycerine	41120	mcg/min	IVC
	norepinphrine	42120	mcg/min	IVC
	procanamide	51130	mg/min	IVC
	xylocaine	52110	mg/min	IVC
Miscellaneous	asa	13220	mg	PO
	adalat	41310	mg	PO
	ativan	82230	mg	SL
	atropin	32110	mg	IV
	calcium chloride	56150	mg	IV
	captopril	41410	mg	PO
	digoxin	23110	mg	IV
	ephedrine	22330	mg	IV
	lasix	11310	mg/hr	IV
	librium	82280	mg	PO
	magnesium sulphate	56110	gm	IV
	meperidine	82120	mg	IM
	midazolam	82210	mg	IV
	morphine	82110	mg	IV
	nitro-paste	41129	in	T
	percocet	82140	tabs	PO
	potassium chloride	56120	mEq	IV
	sodium bicarbonate	61210	mEq	IV
	tylenol	82160	mg	PO
	valium	82220	mg	IV
	ventolin	91110	mL	IN
	verapamil	31210	mg	IV
	vitamin K	13150	iu	IV
	2/3-1/3 plain	12230	mL	IVC
	2/3-1/3 with KCl	12240	mL	IVC
	d5w flush	12250	mL	IVC

Table 11. A list of therapeutic agents and their codes used in the study. Legend: IVC-intravenous continuous; IV-intravenous bolus; IN-inhalant; IM-instramuscular; PO-per oral; SL-slow release; T-topical.

7.2.7 Drug-Dosage Response Tables

Central to the conceptual framework of therapeutic management is an ability to predict the hemodynamic response were a specific agent instituted. The approach used in this study involved a set of computational drug-dosage response tables constructed through knowledge acquisition. These tables are used to determine the expected effects of agents on the hemodynamic parameters at different dosage levels. The selection of any agent and its dosage is then based on which would give the best expected response. Two steps were involved in formulating the drug-dosage tables; first, a set of empirical tables was constructed; second, computational tables were then derived using the knowledge from the empirical tables. The two steps are described below.

Empirical Drug-Dosage Response Tables

Through the two experts, the empirical drug-dosage response tables for therapeutic agents commonly used in the CVICU were constructed. First, the common dosage levels for each agent were grouped into three categories of low, medium and high (some agents, such as dopamine, were assigned an additional category of very-low dose). Second, based on their clinical experience, the experts rated the percentage response of the hemodynamic parameters when the agent was given at the specified dosage range (the parameters being HR, ABPS, ABPM, MAP, SVRI, PAPS, PAPM, PAPD, PVRI, CI, PAWP, CVP, SI and URINE). A numerical scale of -3 to +3 was used to indicate the magnitude of percentage response expected, being: -3 for >30% reduction, -2 for 16 to 30% reduction, -1 for 5 to 15% reduction, +1 for 5 to 15% increase, +2 for 16 to 30% increase, +3 for >30% increase, and 0 for no change. These empirical drug-dosage tables formed the basis for computing the expected hemodynamic response at different dosage levels. Examples from the empirical drug-dosage tables are in Table 12; the complete set is in Appendix E.

AGENT	Dose	HR	APS	APD	MAP	SVRI	PAS	PAM	PAD	PVRI	CVP	WP	CI	Urine
Dopamine	0.5-5	1	0	0	0	0	0	0	0	0	0		1	1
	6-10	1	1	1	1	1	0	0	0	0	1	1	2	2
	11-20	2	2	2	2	2	1	1	1	1	1	2	3	2
	>20	3	3	3	3	3	2	2	2	2	2	2	2	1
Nipride	<1	0	-1	-1	-1	-1	0	-1	-1	0	-1	-1	1	0
	1-4	-2	-2	-2	-2	-1	-1	-1	-1	-1	-2	-2	2	0
	>4	1	-3	-3	-3	-3	-1	-1	-1	-1	-2	-3	2	0
Albumin-5	100	-1	1	1	1	0	0	0	0	0	1	1	1	1
Albumin-5	250	-1	1	1	1	0	0	0	0	0	1	1	1	1
Crystalloid	1000	-1	1	1	1	0	0	0	0	0	1	1	1	1

Table 12. Examples of empiric drug-dosage response tables based on clinical experience of the expert CVICU physicians. Legends: HR-heart rate; APS-arterial pressure systolic; APD-arterial pressure diastolic; MAP-mean arterial pressure; SVRI-systemic vascular resistance index; PAS-pulmonary arterial systolic; PAD-pulmonary arterial diastolic; PAM-pulmonary arterial mean; PVRI-pulmonary vascular resistance index; CVP-central venous pressure; WP-wedge pressure; CI-cardiac index. Dosages are expressed in mcg/kg/min for dopamine, mcg/min for nipride and mL for albumin and crystalloid. For the numeric coding scheme, see text in section 7.2.7 on empirical drug-dosage response tables.

Computational Drug-Dosage Response Tables

To formulate the computational tables, the expected effects of each therapeutic agent were interpolated based on the common dosage levels from the empirical drug-dosage tables. The assumption was that drug-dosage response follows a log-linear relationship for the dosage levels being considered (Gibaldi 1984). The computational tables allow one to predict the hemodynamic value based on the its current value and the expected effect at a given dosage level for that parameter. The formulation of the computational tables is described below.

First, the low, medium and high dosage ranges for each agent from the empiric dosage tables were expanded to include common dosage levels encountered in the clinical setting; the logarithm of each of these dosage levels was then determined. Second, based on the known percentage responses for an agent and its dosages, the expected effect (expressed in fractions) was interpolated for each of the remaining dosage levels. To illustrate, there are four dosage levels of 5% albumin: 100, 200, 250 and 500 mL. The logarithms of these levels are 2.00, 2.30, 2.40 and 2.70, respectively. It is known that 500 mL would bring about a 20% increase in HR, MAP and CVP. Since 100 mL has a minimal effect of 5%, the lower and upper extremes of the expected effects become 0.05 and 0.20 (in fractions), which correspond to the logarithmic range of 2.00 and 2.70, respectively. Linear interpolation yields the expected effects for the remaining dosage levels of 200 and 250 mL. The computational drug-dosage response tables for albumin and nipride are shown in Table 13; the complete set is in Appendix F. A complete list of therapeutic agents with their drug-dosage responses defined is shown in Table 14.

AGENT	Dose	Log	HR	APS	APD	MAP	SVRI	PAS	PAM	PAD	PVRI	CVP	WP	CI	Urine
Albumin	100	2.0	-.1	.05	.05	.05						.05	.05	.05	.05
	200	2.3	-.1	.12	.12	.12						.12	.12	.12	.12
	250	2.4	-.2	.15	.15	.15						.15	.15	.15	.15
	500	2.7	-.2	.2	.2	.2						.2	.2	.2	.2
Nipride	0.2	-0.7					-.05					-.05	-.05	0.1	
	0.4	-0.4					-.10					-.13	-.13	.10	
	0.6	-0.2					-.13					-.18	-.18	.13	
	0.8	-0.1					-.15					-.21	-.21	.15	
	1	0.0	0.0	-.05	-.05	-.05	-.17	-.05	-.05	-.05	-.05	-.16	-.16	.16	
	2	.30	.06	-.15	-.15	-.15	-.22	-.15	-.15	-.15	-.15	-.27	-.27	.21	
	4	.60	.12	-.24	-.24	-.24	-.27	-.24	-.24	-.24	-.24	-.38	-.38	.27	
	6	.78	.15	-.3	-.3	-.3	-.3	-.3	-.3	-.3	-.3	-.45	.3	.3	

Table 13. The computational drug-dosage response tables for albumin 5% and nipride. The expected effects are computed by interpolating from the extreme low and high values against the logarithmic values of the respective drug-dosages. The expected effects are expressed in fractions. The empty cells represent no effect for that hemodynamic parameter. Dosages are in mL for albumin and mcg/min for nipride.

albumin-5	100, 200, 250, 500 mL
albumin-25	50, 100, 200 mL
amrinone	0.05, 2, 4, 6, 8, 10, 12, 18 mcg/kg/min
ativan	2, 4, 6, 8, 10 mg
atropin	0.5, 1, 1.5, 2, 3 mg
autotransfusion	100, 200, 300, 400, 500 mL
bretylium	2, 4, 6, 8 mg/hr
captopril	6, 12, 15, 20, 50 mg
d5w	100, 200, 250, 500, 750, 1000 mL
digoxin	0.1, 0.2, 0.4, 0.6, 0.8, 1 mcg/min
dobutamine	2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 30, 40 mcg/kg/min
dopamine	2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 30, 40, 50 mcg/kg/min
edrophonium	1, 5, 10, 15 ug/min
ephedrine	10, 15, 20, 25, 30, 40 mcg/kg/min
epinephrine	0.2, 0.4, 0.6, 0.8, 1, 2, 4, 6, 8, 10, 20, 25 mcg/min
fresh-frozen-plasma	100, 200, 300, 400, 500 mL
isuprel	1, 2, 4, 6, 8, 10, 20, 30 mcg/min
labetalol	1, 2, 4, 8, 10 mg/hr
lasix	5, 10, 15, 20, 25, 30, 40 mg/hr
librium	5, 10, 20, 40, 60 mg
meperidine	25, 50, 75, 100, 150 mg
midazolam	2, 4, 6, 8 10 mg
morphine	2, 4, 6, 8, 10 mcg/min
nitro-paste	1, 2, 3, 4, 6 in
nitroglycerine	0.2, 0.4, 0.6, 0.8, 1, 2, 4, 6 mcg/min
nifedipine	10, 20, 30 mg
nipride	0.2, 0.4, 0.6, 0.8, 1, 1.2, 1.4, 1.6, 1.8, 2, 2.4, 2.8, 3.2, 4 mcg/min
norepinphrine	1, 2, 4, 6, 8, 10, 15 mcg/min
normal-saline	100, 200, 250, 500, 750, 1000 mL
packed-cells	100, 200, 300, 400, 500 mL
percocet	2, 4, 6, 8, 10 mg
procanamide	2, 4, 6, 8 mg/min
propanolol	0.5, 1, 2, 3, 4 mg/hr
ringers	100, 250, 500, 750, 1000 mL
verapamil	1, 2, 4, 6, 8, 15 mg
xylocaine	2, 4, 6, 8 ug/min

Table 14. A complete list of therapeutic agents included in the study with their respective dosage levels.

7.2.8 Reverse Protocols

Reverse protocols are essentially the same as therapeutic protocols, except in the way they are invoked. In reverse protocols, one takes an actual intervention instituted and looks to see if all of the criteria justifying the intervention were present (the therapeutic protocols start with the clinical condition and then propose the intervention under the protocol rule that best matched the condition). In the study, reverse protocols were developed to critique the use of packed cells, albumins, ringers, D5W, cryoprecipitate, protamine, platelets, fresh-frozen plasma, protamine, amicar, bicarbonate, Mg, K and Ca. An example of a reverse protocol is in the use of packed cells and fresh-frozen plasma, which would be critiqued if not for conditions of low HCT/HB and/or high CT loss with coagulopathies. The development of reverse protocols was simplified by the therapeutic protocols that were already formalized – the conditions and the therapy recommendations for each protocol rule could be simply reversed. Examples of reverse protocols are in Table 15; the complete set is in Appendix G.

11.2 if intervention-choice = packed cells
then
(HCT within last 12 hours < 24) or (HB within last 12 hours < 8)
ICU-admission since surgery <= 5 hours

11.3 if intervention-choice = ringers lactate or normal saline
then
(OSM within last 6 hours >= 280) and (OSM within last 6 hours <= 300)
weight-gain < 10% admission-weight
(serum Na within last 6 hours >= 135) and (serum Na within last 6 hours <= 150)
(URINE > 1 ml/kg/hour) or (URINE < 1 ml/kg/hour)
(I/O-balance < -1 litre) or (I/O-balance > -1 litre)
condition is not ARDS and COPD
crystalloid-therapy not failed

11.8 if intervention-choice = protamine
then
condition = active-bleeding
PTT > 40

11.9 if intervention-choice = platelets
then
condition = active-bleeding
platelets < 40,000

Table 15. Examples of reverse protocols.

7.3 Reasoning and Control

As distinct from the inferencing mechanism of classical expert systems, which use a non-deterministic or opportunistic approach (Buchanan 1985), the reasoning and control formalism adopted in our system is entirely deterministic. The reasoning processes discussed in this section are: interpreting the data; prediction; net-difference scoring and ranking; adjustment in dosage levels; combining effects of multiple agents; planning the interventions; reasoning over time; weaning patients from medications; redefining target ranges; updating the patient-specific drug-dosage response tables.

7.3.1 Interpreting the Data

Interpreting the patient data is the first processing step that involves validating the data, constructing the patterns and matching the constructed patterns to known patterns, conditions and/or intervention strategies. Because of the inherent fluctuations in individual hemodynamic signals, it is preferable to use averaged readings. In the study, we chose the median value over five minutes as the basic real-time resolution of the hemodynamic data actually available every minute. The median is less susceptible than the mean to extreme values, and unlike the mode, can always be derived. This approach was deemed realistic within a clinical setting, since the degree of resolution is as good as the frequency of manual assessment in the CVICU, which ranges from every 15 minutes to one hour. Averaging the data also reduced the processing load on the system.

Each parameter value is checked for the physiologic range limits. Several cross-validation rules are used. Examples of violating cross-validation are when HR differs from PULSE by more than 10%, PAWP is greater than PAD, and direct MAP reading differs from recomputed MAP[1] by more than 10%. Any PAWP available as part of the cardiac output assessment prompts discarding of the PAD from pattern-matching if the two differ by more than 4 mmHg. Alert messages are generated on any data that failed the validation.

7.3.2 Prediction

Judgment of the patient's progress at any time point must be based on expectations, i.e. on a prediction of values. The therapeutic recommendations at any instant are also based on their expected effects. Hence, prediction is an essential part of this system. For predicting the hemodynamic values when there was no change to existing therapies, the technique of exponential smoothing averaging (ESA) was used (Buffa 1987). The method to predict the effects of a changed therapy on hemodynamic values is net-difference scoring, which is addressed later (see section 7.3.3). The ESA model is shown as follows:

Current base = α(Current value) + $(1-\alpha)$(Previous base) or, stated in symbols,

$$S_t = \alpha D_t + (1-\alpha)S_{t-1}$$

---

[1] Recomputed MAP = (ABPS + (ABPD x 2)) / 3

where the smoothing constant, α, which controls the weighting of the current value, was chosen to be 0.3 in the study. Using this model, the computed current base, or S_t, will become the forecast value for the next period. For example, we could predict the MAP value over the next 15 minutes using the current MAP and the previous base MAP, with an alpha value of 0.3. The current base MAP is then used as the predicted value for the next period. The predicted values can be used to form the predicted hemodynamic status pattern, which can be matched to the clinical conditions for interpretation.

7.3.3 Net-Difference Scoring and Ranking

The net-difference score, or net-score, is a composite index of how much the hemodynamic parameters deviate from the respective target ranges. The closer the hemodynamics to the target ranges, the lower the net-score, zero being totally within range. The parameters used are HR, ABPS, ABPM, MAP, SVRI, PAPS, PAPM, PAPD, PVRI, CI, PAWP, CVP and SI. The net-scoring approach provides an objective means of assessing the patient's state – a patient having a zero net-score is considered as having achieved the targets. The approach also allows one to compare between patient states and the effects of therapies by ranking the respective scores. The ranking algorithm takes the net-scores of all alternative therapeutic agents at different dosages and ranks them in increasing magnitude. The agent/dosage with the minimal score is the preferred choice, since by instituting the agent/dosage the hemodynamics should get closest to the target range.

To compute the net-score, the current hemodynamic values are compared with their respective target range. For each parameter, the score is zero if the value is within target range, otherwise it is the difference between the value and the nearest target figure, i.e. the nearer warning threshold. Since the parameters vary in their numeric scales, the difference is normalized as a percentage of the corresponding target figure. The direction doesn't matter, any minus sign is ignored. Thus, a MAP of 65 mmHg and a target range of 70 to 85 mmHg represents a difference of -5 mmHg, a normalized difference of 7%. Finally, to emphasize the greater difference, the normalized score is multiplied by a weighting factor, currently set at 1 for warning, 2 for alert and 3 for critical thresholds. This process is repeated with each parameter and finally these individual values are summed as the net-difference. A second normalization can be done to prorate the score based on the number of parameters present, to allow intermittent measures such as cardiac output to be compared directly with the continuous parameters. However, this second normalization was found to have questionable utility and subsequently ignored during the study, since it had rendered the resulting net-score difficult to interpret.

To compute the net-score when a therapeutic agent is considered, the current hemodynamic values are first multiplied by the expected effects in the computational drug-dosage table for the desired agent/dosage. Dynamic interpolation of the dosage-effects is done automatically if the desired dosage is not in the knowledge base. The interpolation is done using the dosage and effect values adjacent to the desired dosage and applying the same log-linear computation algorithm used to construct the initial drug-dosage response tables. These adjusted hemodynamic values are then compared with their respective target range as in the net-scoring algorithm described above. The resulting net-score represents how close the parameters would be from the target range if the agent at the specified dosage were instituted.

To be precise, one should take into account the time required for the agent to take effect, its half-life, maximum effect, the duration of residual effect when discontinued, contraindications, side-effects and interactions. In our study, all of the agents were assumed to achieve their maximal effect within 15 minutes of administration. Also assumed were the absence of side-effects, contraindications and interaction effects. An example calculation of the net-score is shown in Table 16 where nitroglycerine of 1 mcg/min is being added.

Another assumption was that residual effect of an agent could be ignored. Such analgesic agents as morphine, which can have a residual effect lasting two hours or longer, are exceptions. For all analgesics, the expected effect is prorated by interpolating between the current effect and the logarithm of the residual effect duration in hours. In the example of morphine, since it can lower MAP and HR, one must take into account morphine's residual effect once discontinued when computing the net-score of another agent being instituted.

(a)	HR	APS	MAP	APD	SVRI	PAD	PAM	PAS	PVRI	WP	CVP	CI	SI	
Target-L	60	60	70	100	2000	6	6	15	255	6	6	2.2	33	Pattern
Current=>	94	67	94	114	2192	26	33	42	260	24	20	2.7	27	44476
Target-H	10	90	100	140	2400	16	16	30	285	16	16	3.5	47	
Difference	0	0	0	0	0	10	17	12	0	8	4	0	-6	Net-Diff
Diff %	0	0	0	0	0	63	106	40	0	50	25	0	-18	266
(b) Now add - Nitroglycerine @ 1ug/kg/min														
Effect%	0	-10	-10	-10	-10	-15	-10	-10	-10	-16	-16	16	16	
Predict=>	94	60	85	103	1863	22	30	38	234	20	17	3	31	
Difference	0	0	0	0	-137	6	14	8	21	4	1	0	2	Net-Diff
Diff %	0	0	0	0	-7	42	86	26	-8	26	5	0	-5	165

Table 16. Anticipated hemodynamic effects of adding nitroglycerine at 1 mcg/min. Opt-L and Opt-H are the optimal lower and upper range for each of the parameters. The Difference is obtained by subtracting the current/predict value from the range, and Diff% represent the Difference score normalized according to its lower/upper range. The Net-Diff is simply the summation of the individual Diff%.

7.3.4 Adjustment of Dosage Levels

Where a new therapeutic agent is added, the computation of the net-score is done as outlined. However, often the dosage level of an agent is adjusted up or down once it has already been started, or that the agent is discontinued altogether. With such changes, the dosage response must be adjusted differently, depending on whether the expected effects would increase or decrease the parameter value.

Two heuristics were developed; the first deals with an increase in the dosage of an agent. If the expected effects for that agent are proportional to the dosages, the result is simply the difference between the effects under the new and old dosage. For instance, if the patient has already received 250 mL of albumin, and the dosage effects for albumin at 250 and 500 mL are 15% and 20%, respectively, then by giving an additional 250 mL of albumin, another 5% change in hemodynamic effects is expected. The heuristic also applies to situations where the expected effect is inversely proportional to the dosage levels, and when the drug-dosage is reduced or discontinued. A second heuristic applies to reducing any agents with positive expected effects, as in the case of weaning the patient from inotropes. In such instance, there is zero expected effect from the reduction in dosage. The assumption was that the body can sustain the physiologic effects brought on earlier by the agent despite the diminishing drug effect from the decrease in dosage. Examples of how the heuristics are applied under different situations are shown in Figure 20.

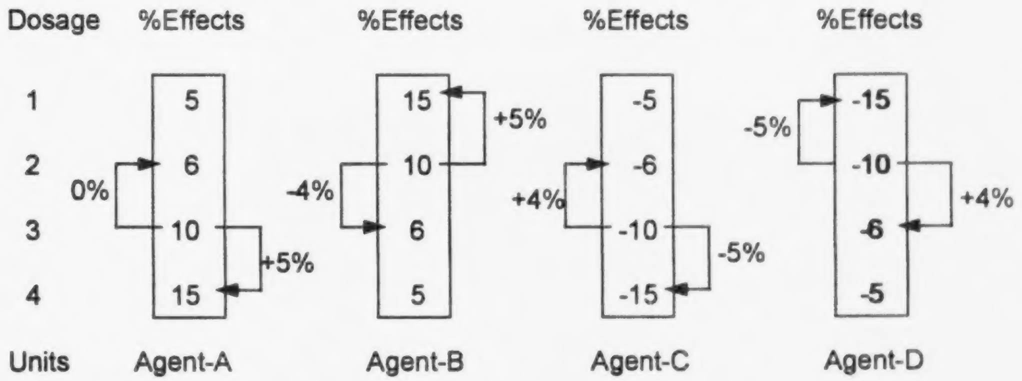


Figure 20. Examples of new dosage effects as a result of changes in dosage level of the therapeutic agents. In Agent-A, a decrease in dosage will result in 0 expected effect change; this is assuming the body will sustain the positive effect brought on earlier at the original higher dosage level. This is often the case with positive inotropes such as dopamine. Agent-B represents the typical plateau effect often seen on CI and urine when dopamine is given at high doses. Agent-C is typical of vasodilators such as nitroglycerine. Low-dose dobutamine exerts a negative but diminishing effect on SVRI similar to that described in Agent-D. The dosage units are arbitrary.

7.3.5 Combining Effects of Multiple Agents

Often the CVICU patient is on two or more active therapies, being fluids, inotropes and/or vasoactive agents. The interacting effects of these agents are complex and dynamic, depending on the condition, dosage level and pharmacodynamics. In this study, two additional heuristics were developed to allow to combine the expected effects on the hemodynamic parameters when multiple agents were involved.

One heuristic is that if there was no change to an existing agent, the expected effect for each of the hemodynamic parameters would remain as zero. This assumed that the agents would reach maximal effects within 5 minutes of institution and sustain a plateau effect for as long as the agent is being infused at the current dosage level. When multiple agents are adjusted at the same time, the min-max heuristic is used. This heuristic applies to agents to be added, continued at different dosages, or discontinued but with residual effect. Specifically, the maximum expected effect of a parameter is used if all of the agents exert some effects on that parameter in the same direction. For opposing effects, the difference from all the opposing expected effects on a parameter is used. For example, if both dobutamine at 2 mcg/kg/min and nitroglycerine at 1 mcg/min were to be administered, for those parameters where the expected effect between the two agents are similar in magnitude, the larger of the two is used. If the expected effects of the two agents for a given parameter are opposing, the difference of the two effects is used. An example of this computation is shown in Table 17.

(a)	HR	DBP	MAP	SBP	SVRI	PAD	PAM	PAS	PVRI	WP	CVP	CI	SI	
Target-L	60	60	70	100	2000	6	6	15	255	6	6	2.2	33	Pattern
Current=>	94	67	94	114	2192	26	33	42	260	24	20	2.7	27	44476
Target-H	110	90	100	140	2400	16	16	30	285	16	16	3.5	47	
Difference	0	0	0	0	0	10	17	12	0	8	4	0	-6	Net-Diff
Diff %	0	0	0	0	0	63	106	40	0	50	25	0	-18	266
(b) Now add - Dobutamine @ 2ug/kg/min														
Effect%	0	-10	-10	0	-10	-10	0	0	0	0	0	10	10	
(c) Now add - Nitroglycerine @ 1ug/kg/min														
Effect%	0	-10	-10	-10	-10	-15	-10	-10	-10	-16	-16	16	16	
(d) Combined effects of Dobutamine and Nitroglycerine														
Effects%	0	-10	-10	-10	-10	-15	-10	-10	-10	-16	-16	16	16	
Predict=>	94	60	85	103	1863	24	30	38	234	20	17	3	31	
Difference	0	0	0	0	-137	8	14	8	21	4	1	0	2	Net-Diff
Diff %	0	0	0	0	-7	46	86	26	-8	26	5	0	-5	169

Table 17. The anticipated hemodynamic effects of instituting two agents simultaneously. In this example, dobutamine at 2ug/kg/min and nitroglycerine at 1ug/kg/min, are computed and shown in terms of their net difference from the optimal ranges and the cumulative effect of instituting the agents. Optimal-L,-H, and Current=> represent the optimal therapeutic ranges and hemodynamic values currently under evaluation. Note that the expected effects for PAD are -10% and -15% for dobutamine and nitroglycerine, respectively. According to the max-min heuristic, the net effect becomes -15%.

7.3.6 Planning the Interventions

Planning the interventions involves selecting preferred intervention and critiquing therapies instituted, all within context of the existing condition and the therapies already instituted or proposed. The planning process is shown in Figure 21. During each cycle, the plan to select interventions would begin once the constructed patterns are matched to known patterns and conditions.

Two steps are involved in formulating an intervention plan. First, the constructed patterns are matched to one or more pending strategies. A strategy can be one of: continue monitoring; perform a diagnostic test; select a therapeutic intervention. The time-delay algorithm is used to reconcile and invoke pending strategies. Second, for each strategy invoked, an intervention choice is selected; the ranking algorithm is used to select from alternative agents/dosages if appropriate.

For electrolyte-replacements and diagnostic tests, the choice is specified directly by the invoked strategy. Fluids and bleeding treatments are guided by protocols. For instance, the agent used to treat bleeding depends on the levels of PT-INR, PTT and PLT. The amount of fluid is determined by the net-scoring and ranking algorithms. For critiquing, there are five scenarios:

- If the patient is on vasoactive therapy, the net-scoring and ranking algorithms would be invoked during each cycle to critique possible changes in dosage.
- Any time there is a change in an actual inotropic or vasoactive therapy, the net-scoring and ranking algorithms are invoked to critique the appropriateness of the change; an alternative dosage is proposed if it has better hemodynamic responses than the dosage being changed.
- Reverse protocols are applied to therapies to see if they met the criteria justifying their use; currently, all therapies instituted are checked except for inotropes and vasoactive agents.
- The opportunity to wean inotropes and vasoactive agents is explored during each cycle, and weaning is proposed if the predefined criteria are met (see section 7.3.8).
- The target range for HR, MAP, CVP, PAD and PAWP are checked during each cycle for redefinition; if required, the ranges are automatically redefined and a message is issued (see section 7.3.9).

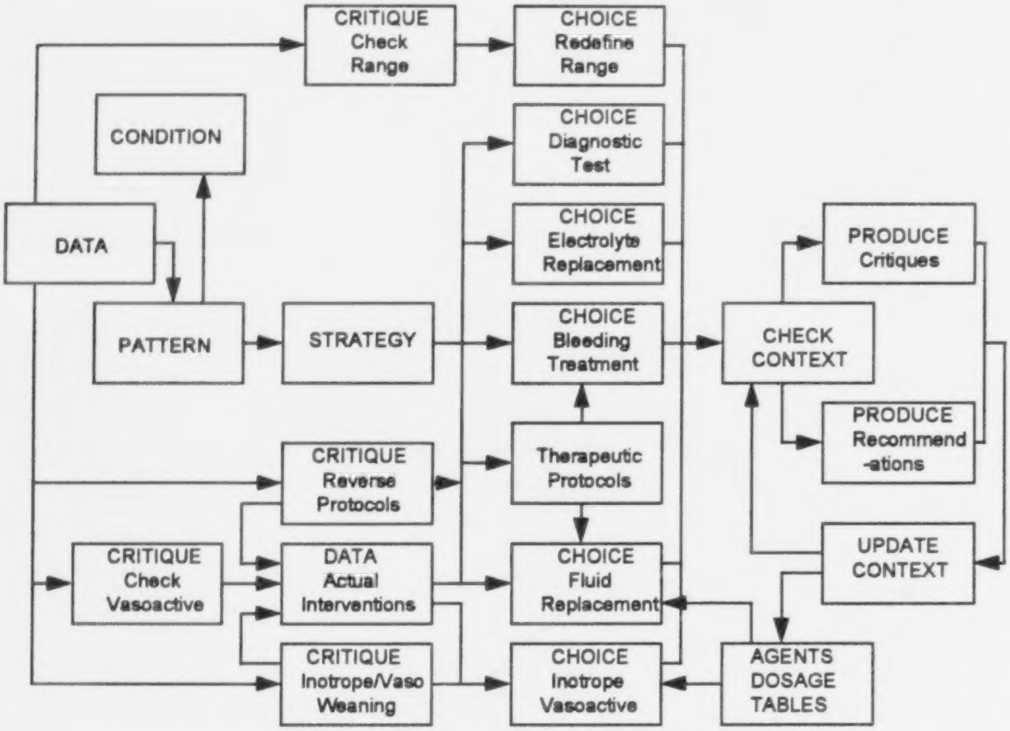

CRITIQUE Check Range
CHOICE Redefine Range
CONDITION
CHOICE Diagnostic Test
DATA
CHOICE Electrolyte Replacement
PRODUCE Critiques
PATTERN
STRATEGY
CHOICE Bleeding Treatment
CHECK CONTEXT
PRODUCE Recommend -ations
CRITIQUE Reverse Protocols
Therapeutic Protocols
UPDATE CONTEXT
CRITIQUE Check Vasoactive
DATA Actual Interventions
CHOICE Fluid Replacement
CRITIQUE Inotrope/Vaso Weaning
CHOICE Inotrope Vasoactive
AGENTS DOSAGE TABLES

Figure 21. The process of planning the interventions.

Before producing the output, each intervention choice is compared with the patient's current context. For example, if the choice is to administer 1000 mL of ringers lactate, but the patient has already received ringers, or ringers had already been proposed earlier, then the recommendation would be appropriately annotated. What remain are opportunities not exploited or problems not investigated. The instituted and proposed interventions from the most recent two hours are always kept in context. An arbitrary criterion on redundant recommendations was set; specifically, if an intervention choice has already been proposed or actually instituted within the last hour, a message is appended to indicate that the displayed recommendation had been proposed/instituted earlier. For therapeutic agents proposed, the expected change in net-score over the next 15 minutes from the current score is displayed in percentage. An interpretation of the condition expected in the next time period is provided (see next section). The percentage change and interpretation summarize the overall expected impact of the recommendations and critiques on the patient's condition.

7.3.7 Reasoning Over Time

An important part of reasoning is the timing for selecting intervention strategies. A time-delay algorithm was developed to deal with pending severity-dependent strategies, such as check-lines-in-5-minutes and reduce-volume-deficit-in-10-minutes. Within the study, the time delays were set to 10 minutes for patterns with mild severity and 5 minutes with moderate severity. If the change in pattern is severe, the strategy is invoked immediately. For any strategy that has been matched from a constructed pattern, the algorithm decrements this time delay during each cycle until the time becomes 0 minute. Any pending strategy with a 0 minute in its time delay is invoked immediately.

Another role of the time-delay algorithm is to reconcile the timing difference between pending strategies. For example, a hemodynamic status pattern of 53040 from the immediate past state (5 minutes ago) had matched the strategy "reduce-volume-deficit-in-10-minutes", which was still pending. If the current state became 61030, "reduce-volume-deficit-now" would be matched. The algorithm compares the time-delay in both pending strategies and retains the one with a lesser time-delay value. In the example, "reduce-volume-deficit-now" is retained since it has a time delay of 0 minutes.

A state-transition model, shown in Figure 22, is used to facilitate reasoning with the patient data over time. Five distinct states were defined: previous, current, predicted, proposed, target. Each state maintains its own set of physiologic data and net-score. The reasoning is illustrated here starting at stage 2 within the figure:

- The expected hemodynamic effects and the net-score from selecting one or more intervention choices are computed based on the target ranges in the target state and stored in the proposed state.
- The expected effects and net-score from any change in the actual therapy are computed based on the target state and stored in the predicted state; if no change was recorded at stage 2, the exponential smoothing average is used to predict the hemodynamic effects.
- The expected effects and net-score from the previous time period are assumed to be in the previous state.
- The net-scores of the current, predicted, proposed and previous states are compared against each other to determine the overall impact of the proposed and actual interventions. An interpretation is generated based on the comparison.
- The current state becomes the previous state and the cycle starts over again by reading in another set of patient data into a new current state in stage 4.

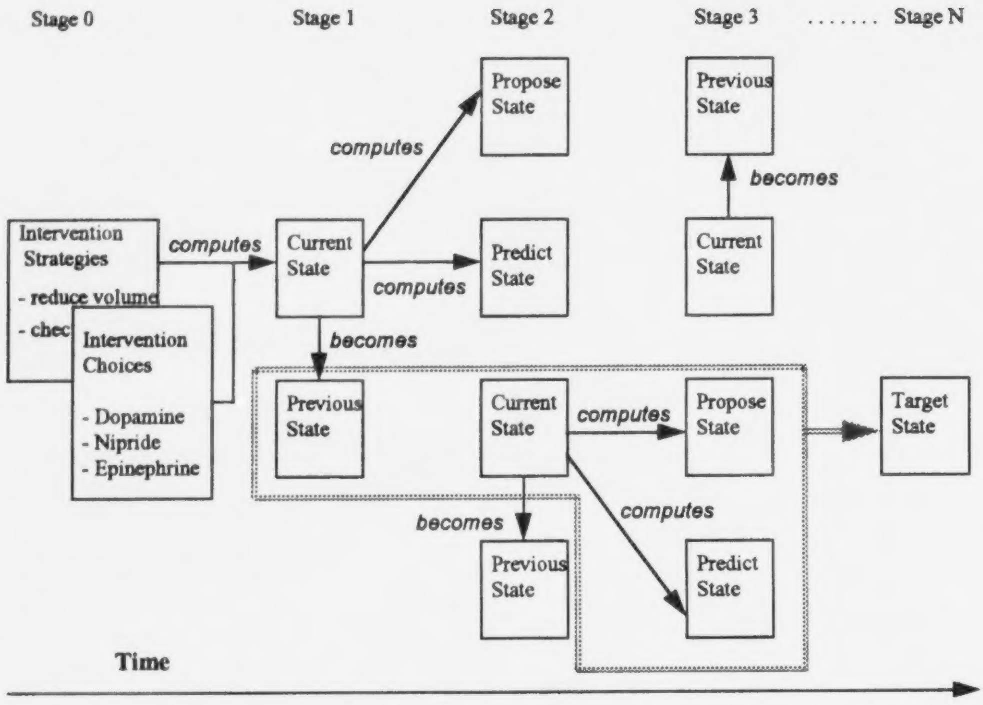

Stage 0
Stage 1
Stage 2
Stage 3
.... Stage N
Propose State
Previous State
computes
becomes
Intervention Strategies
- reduce volume
- chec
Intervention Choices
- Dopamine
- Nipride
- Epinephrine
computes
Current State
Predict State
computes
Current State
becomes
Previous State
Current State
computes
Propose State
Target State
computes
becomes
Previous State
Predict State
Time

Figure 22. A state-transition model used to facilitate reasoning of the patient data over time. The block in the lower half illustrates the comparisons that are done with the states: each of the four states shown in the block is compared with the target state to compute the net-difference score; the net-scores from the four states are also compared with each other to interpret the situation with a meaningful phrase.

The expected impact of any proposed and actual intervention can be determined by comparing the net-scores between the states. For instance, let's assume the net-scores are 30 for the previous state; 20 for the current state; 25 for the predicted state; 6 for the proposed state. The following observations can be made:

- The previous state has the worst score.
- The current state has a lower score than the previous state.
- The predicted state has a higher score than the current state.
- The predicted state has a lower score than the previous state.
- The proposed state has the best score.

An interpretation can be made from the above observations: the patient has improved from the previous state, but the therapy instituted is expected to worsen the condition; instead, the proposed intervention should be instituted, since it is expected to have the most improvement. The interpretation process was generalized during knowledge acquisition; for any comparison, a state can be less than, equal to or greater than another. With six state-pairs each having three outcomes, the permutations are 3^6, but some are inconsistent, leaving only 75 combinations. Examples of the permutations are shown in Table 18. Due to its complexity, this method of interpretation was only partially implemented in the study. Currently, the interpretation is generated based on comparing the current state against the previous, predicted and proposed states.

	Previous	**Current**	**Predicted**	**Proposed**	**Interpretation**
Previous		>	>	>	previous state is worse than all other states
Current	<		>	>	predicted & proposed better than current & previous states
Predicted	<	<		>	predicted better than previous & current but not proposed
Proposed	<	<	<		proposed better than previous, current & predicted states
***Conclusion* =**					proposed is best, condition has improved over previous state
Previous		>	>	>	previous state is worse than all other states
Current	<		<	<	current state better than all other states
Predicted	<	>		<	predicted better than proposed but worse than current state
Proposed	<	>	>		proposed better than previous but worse than others
***Conclusion* =**					condition worsening but proposed is worse, go with predicted
Previous		>	<	<	previous state is better than all other states
Current	>		>	>	current state is worse than all other states
Predicted	>	<		>	predicted better than current, but worse than others
Proposed	>	<	<		proposed better than all but worse than previous state
***Conclusion* =**					condition worsening, proposed and predicted no better

Table 18. Examples of interpretation of the impact of interventions when the net-scores between states are compared. The table reads from left to right with four states plus the conclusion as one set. For instance, in the first set, we have the following interpretations: (a) the net-score of previous state is greater than ones from the current, predicted and proposed states, so the previous state is the worst of all states; (b) the net-score of current state is better than previous but worse than predicted and proposed state, so the therapies in predicted and proposed are effective; (c) predicted state is better than previous and current but worse than proposed state, so the agent in proposed state is the preferred choice; (d) proposed state better than all other states, confirming it is the preferred choice; (e) conclusion states the final interpretation that proposed state has the best choice.

7.3.8 Weaning Patients from Medications

The primary objectives in the CVICU are to stabilize the patient's hemodynamic responses, prevent complications and ensure prompt recovery. Reaching those objectives requires an aggressive approach to discontinuation as well as institution of medications. An example is the weaning of a patient, who has become vasodilated, from nitroglycerine. Current weaning practices for cardiovascular agents used in the CVICU are informal, range from a few hours to 1 or 2 days post-op, depending on the physiologic state of the patient and the clinical impression of the staff.

Because of its complexity, only a modest attempt was made in this study to formalize the weaning of medications. An assumption was that weaning should be pursued as soon as the patient's hemodynamic status pattern has become stable for a predefined period. Candidate agents for weaning were the inotropic and vasoactive agents.

Weaning is considered when, for at least a specified period, the predefined percentage of values from each of the four continuously measured parameters (HR, MAP, CVP and PAD) of the hemodynamic status pattern have remained within the target range for the patient. Two control values are set for each drug – a weaning-instigation period and a within-range percentage. The weaning-instigation period is the minimum period within which the four hemodynamic parameters must remain within the target range before weaning can be considered. The within-range percentage allows for some tolerance on stability; it expresses for each parameter the proportion of values that must be within target range. Based on observations from the critiqued learning cases, the two control values were set at two hours and at 80%, respectively. The settings require no more than 5 exceptions from target range among the 25 5-minutely values of each parameter recorded over the two hours. If this criterion is met by all four parameters, weaning can be instigated.

Since weaning the agent involves a change in therapy, the drug-dosage response computation is automatically invoked to determine the effect of weaning. For instance, if the proposed weaning of nitroglycerine should result in a higher net-difference score than previously obtainable, then weaning is not recommended. This situation can occur when the relevant proportion of hemodynamic parameters were within target range but barely so, allowing the discontinuance of the agent to take enough out-of-range values to violate the minimum requirement.

7.3.9 Redefining Target Ranges

Where previously defined target ranges proved unachievable or unrealistic, it becomes necessary to revise the ranges to accommodate the patient's current condition. This situation occurs in patients with stiff ventricles or active bleeding during the early post-operative period, whose condition subsequently improved, thus requiring range adjustment.

The clinical judgment to redefine the target range is inherently complex, requiring knowledge on the patient's history, pre-, intra- and post-operative conditions, and immediate bedside clinical examination. Ideally, this should be the task of the CVICU physician, since it is not yet feasible to have the system access all of the variables that can influence the decision-making process. Once redefined by the physician, the new ranges can then be recorded in the system to guide future therapies. Since this study was retrospective in nature, it was not possible to ask the staff to assist in redefining the ranges for the historical cases. Hence, only a modest attempt was made to recognize instances where redefinition of the target ranges was warranted. The redefinition applies only to the continuously measured parameters of the hemodynamic status pattern (HR, MAP, CVP and PAD). The algorithm is a modification of the weaning protocol described earlier.

First, an out-of-range percent limit is established; this limit defines the percentage of values outside of the target range permissible within a time period for a hemodynamic parameter. Second, an out-of-range period is also defined; this period determines the length of time within which the out-of-range percent limit is to be applied. In the study, the out-of-range percent limit and out-of-range period were set at 75% and for two hours, respectively. The settings meant if the values of any one of the four hemodynamic parameters remained out of the target range for more than 75% of the time within the past two hours, then we should consider redefining the target range.

At present, only one pair of percent and period limits is used based on observations from the learning cases. The restriction required the parameters to be considered under the same premise. Several default ranges were set up to facilitate the redefinition process. For example, feasible target ranges for MAP are 65-80, 70-85, 75-90, 80-95 and 85-100. A heuristic is used to pick the appropriate range: Take the median MAP value over the last two hours where MAP's had been out of range. For each of the default ranges, determine if the median MAP is at the centre of that range by subtracting it from the lower and upper range limit to see if the two differences are equal. If the median MAP is close to the centre point within a given range, then the two halves on each side of the MAP would be equal or close in magnitude. This range then becomes the newly redefined range for MAP. An alert message is also issued to indicate the change.

7.3.10 Updating the Drug-Dosage Response Tables

While each patient must rely on general drug-dose tables initially, the system provides for these tables to be the starting values for a customized patient-specific drug-dose table. This process involves assessing the effectiveness of each therapeutic agent instituted, and updating the individual's table to render it increasingly patient-specific over time. First, at 15 minutes after any change in therapy, the median values of the hemodynamic parameters are compared with those prior to the change. The difference for each parameter is expressed as a fraction of the original expected effect. For instance, if the original expected effect of 1 mcg/min of nitroglycerine on PAD is -0.1, but it turned out to be only -0.06 when the before and after PAD values were compared, then the original expected effect is updated to -0.06. All other dosage levels are prorated accordingly. This process is repeated for each of the hemodynamic parameters.

Subsequently, if there is another dosage change on the same agent, the same calculation is repeated to determine the new expected effect. However, one has to average this newly derived expected effect with its counterpart obtained earlier. Referring to our previous example, if the next adjustment of nitroglycerine from 1 to 2 mcg/min only brought about a -0.04 change, the newly computed value is averaged with the -0.06 obtained earlier to become -0.05. The same calculation is applied to the other dosage levels as well. This ad-hoc approach to resolving drug-dosage response variations is simplistic but it was a practical means of incorporating individual differences in drug-dosage response over time. This concept of customizing the generic drug-dosage response tables over time within a patient's context is further illustrated in Figure 23.

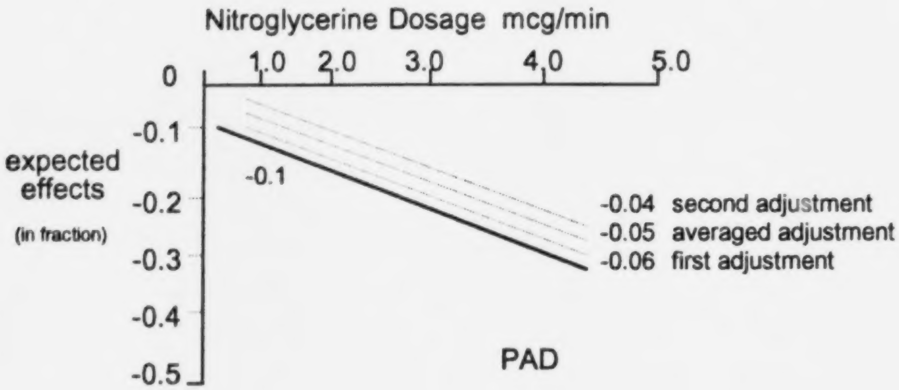


Figure 23. The dosage effect customization for PAD at 1.0 mcg/min of nitroglycerine. The first adjustment resulted in only -0.06 expected effect, whereas the second adjustment is -0.04. The dosage effect update algorithm requires the two to be averaged, giving -0.05 as the final expected effect for PAD at 1 mcg/min of nitroglycerin.

7.4 The Technical Design

The technical design of the decision-support system prototype is summarized in this section. The section covers the prototype's system architecture, historical data files, modes of operation and types of output. Detailed technical design of the prototype in ARTIM code is in Appendix H.

7.4.1 System Architecture

The prototype's system architecture has five components: domain knowledge base; model base; patient data base; reasoning and control rules; user interface. The contents of each component are summarized as follows:

- The domain knowledge base contains the known physiologic patterns, conditions and intervention strategies and choices, the standard reference ranges, the therapeutic agents and their dosage effects, and the therapeutic protocols.
- The model base consists of computational models, functions and variables used such as the exponential smoothing average, and the net-difference scoring and ranking algorithms.
- The patient data base maintains the patient's clinical data being analyzed, which are the hemodynamics, blood gases, fluid intake-output, laboratory data and therapeutic interventions. Also included are the different patient states, customized reference ranges, interpretations, interventions and active selections derived by the system during the reasoning process.
- The reasoning and control rules are procedural in nature and are used to drive the reasoning process in a deterministic fashion.
- The user interface consists of rules and functions used to prompt the user for input and to display output. The standard ARTIM studio windows interface is also used to provide an

interactive explanations environment for justifying rule invocations and viewing the knowledge base during the analysis of a historical CVICU case.

Even though the terms knowledge and model bases are used, they are only text-files loaded into the ARTIM program during execution. As such, no external data, model or knowledge-base management system was used. The five components of the prototype are shown in Figure 24.

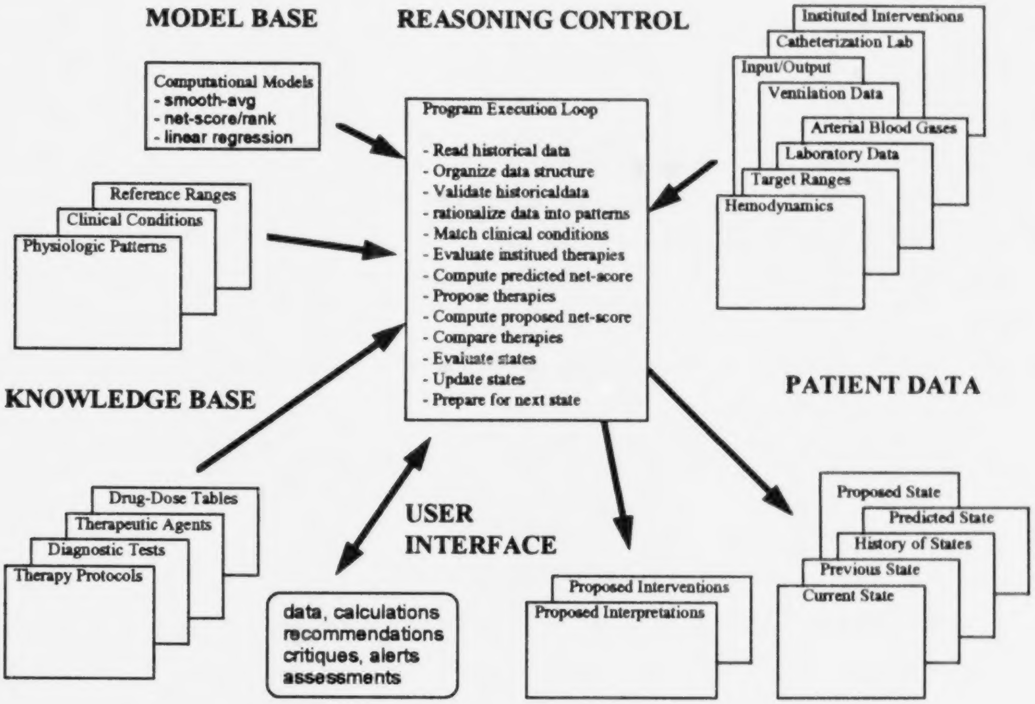

MODEL BASE
REASONING CONTROL
Computational Models
- smooth-avg
- net-score/rank
- linear regression
Program Execution Loop
- Read historical data
- Organize data structure
- Validate historicaldata
- rationalize data into patterns
- Match clinical conditions
- Evaluate instituted therapies
- Compute predicted net-score
- Propose therapies
- Compute proposed net-score
- Compare therapies
- Evaluate states
- Update states
- Prepare for next state
Instituted Interventions
Catheterization Lab
Input/Output
Ventilation Data
Arterial Blood Gases
Laboratory Data
Target Ranges
Hemodynamics
Reference Ranges
Clinical Conditions
Physiologic Patterns
KNOWLEDGE BASE
PATIENT DATA
Drug-Dose Tables
Therapeutic Agents
Diagnostic Tests
Therapy Protocols
USER INTERFACE
data, calculations
recommendations
critiques, alerts
assessments
Proposed Interventions
Proposed Interpretations
Proposed State
Predicted State
History of States
Previous State
Current State

Figure 24. The five major components of the prototype. The direction of the arrows indicates whether the data/mode/knowledge is used or created.

7.4.2 Historical Data Files

The patient data from all historical CVICU cases – hemodynamics, intake-output, laboratory and blood gases results and therapeutic interventions – were stored as text-files. Data recorded at the same time had the same collection date/time stamp and were considered a set. Each historical case had four files: the hemodynamics at 1-minute intervals; the customized target ranges from the expert physician; the laboratory, blood gas and intake-output data; the therapeutic interventions (consisted of agent name, dosage, and date/time started and stopped). Examples of the files are shown in Table 19. A system configuration file was used to specify run-time characteristics, such as whether or not to update the general drug-dosage response tables.

Hemodynamics	**Laboratory**	**Actual therapies**
DATE 14-MAY-91	DATE 14-MAY-91	START-DATE 14-MAY-91
TIME 1155	TIME 1200	START-TIME 1200
HR 105	MODE IMV	THERAPY-CODE 223100
ABPS 113	VRATE 8	DOSAGE 4.6
ABPD 48	FIO2 70	STOP-DATE 14-MAY-91
ABPM 153	O2SAT 98	STOP-TIME 1559
END	CT 15	END
DATE 14-MAY-91	URINE 30	START-DATE 14-MAY-91
TIME 1156	END	START-TIME 1130
HR 106	DATE 14-MAY-91	THERAPY-CODE 122400
ABPS 102	TIME 1210	DOSAGE 50
ABPD 61	MODE IMV	STOP-DATE 14-MAY-91
ABPM 72	PO2 178	STOP-TIME 1200
PAPS 19	PCO2 32	START-DATE 14-MAY-91
PAPD 14	H 35	START-TIME 1130
PAPM 16	SAO2 99	THERAPY-CODE 122500
VPB 1	BASE 1	DOSAGE 27
END	WBC 10.0	STOP-DATE 14-MAY-91
DATE 14-MAY-91	HB 9.0	STOP-TIME 1200
TIME 1157	HCT 26	START-DATE 14-MAY-91
HR 105	PLT 151	START-TIME 1130
ABPS 104	PT 1.4	THERAPY-CODE 12230
ABPD 57	PTT 26.7	DOSAGE 10
ABPM 70	NA 139	STOP-DATE 14-MAY-91
PAPS 20	K 4.0	STOP-TIME 1200
PAPD 15	CL 108	START-DATE 14-MAY-91
PAPM 18	CO2 23.2	START-TIME 1200
VPB 1	OSM 293	THERAPY-CODE 41120
END	BUN 3.6	DOSAGE 0.9
DATE 14-MAY-91	CREAT 69	STOP-DATE 15-MAY-91
TIME 1158	GLU 8.5	STOP-TIME 0634
HR 106	IONCA 1.12	START-DATE 14-MAY-91
APBS 99	CA 2.00	START-TIME 1201
ABPD 57	PHOS 0.47	THERAPY-CODE 12240
ABPM 69	MG 0.64	DOSAGE 50
PAPS 19	CK 436	STOP-DATE 14-MAY-91
PAPD 13	ALB 27	STOP-TIME 1300
PAPM 18	TPROT 47	END
END	END	

Customized Target Ranges

DATE	14-MAY-91	
TIME	1155	
HR	60	120
ABPM	70	85
CI	2.6	3.2
CVP	10	14
PAPD	10	14

Table 19. Sample input data files from a case. Each set of data is separated by an END clause. This allows the system to read in one set of data at a time up to each END marker. Note that the name of the therapeutic agent is codified as a five-digit number. Any change in the dosage of an agent is treated as a new intervention with its own start and stop dates and times.

7.4.3 Mode of Operation

The system operates in a monitoring mode, simulating a real-time environment by reading in one set of patient data at a time and producing recommendations and critiques as appropriate. The system stops when there is no more patient data or when halted by the operator via the ARTIM studio interface commands. The major processing steps of the system are summarized below.

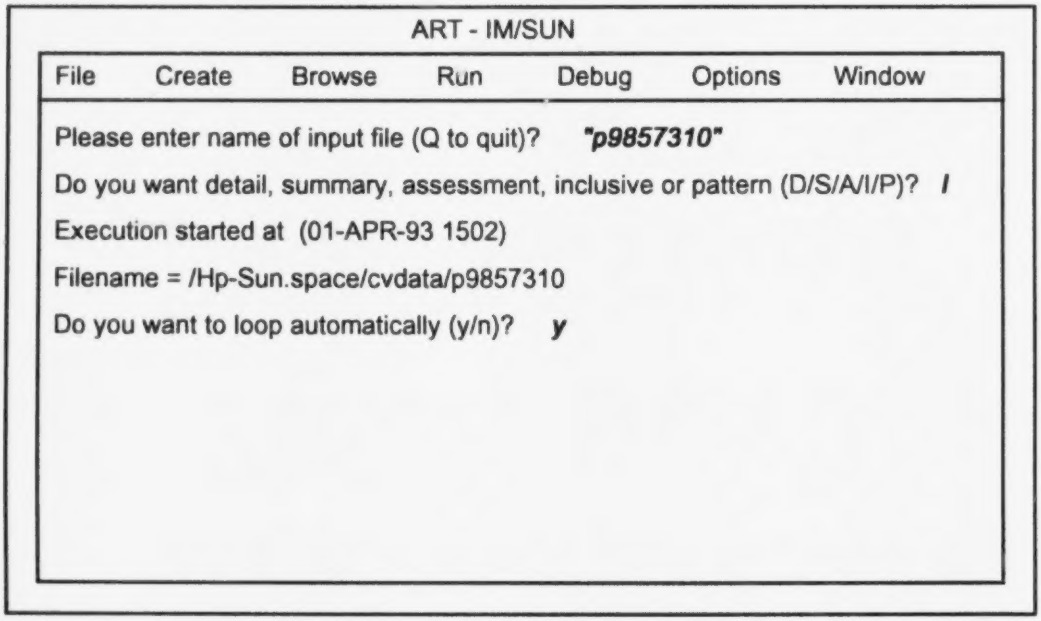
These steps are for initialization only:

- Set up system parameters, e.g. update drug-dosage tables, etc.
- Read in the customized target ranges and update the default reference ranges.

These steps are repetitive:

- Read in the next available set of hemodynamic data.
- Read in any other patient data up to the time-stamp of the hemodynamic data.
- Validate the data in the current state.
- Rationalize the data and construct physiologic patterns.
- Match the constructed patterns to known patterns and conditions.
- Match the classified patterns to intervention strategies.
- Use the time-delay algorithm to rationalize any pending intervention strategies
- Invoke intervention strategies with 0 time-delays to select the intervention choices.
- If the choice is a electrolyte-replacement, check context before recommending.
- If the choice is a fluid, compute net-score for amount; check context before recommending.
- If the choice is a diagnostic test, check context before recommending.
- If the choice is for bleeding, check protocols then context before recommending.
- If the choice is to redefine range, check context before critiquing.
- If vasoactive agent is present, compute net-score for preferred dosage, then check context before critiquing.
- If inotrope and/or vasoactive agent present and dosage changed, compute net-score for preferred dosage, then check context before critiquing.
- Use reverse protocols to check all therapies except for inotropes and vasoactive agents; check context before critiquing.
- For every therapy instituted, assess the actual drug-dosage response and update the general drug-dosage response tables to become patient-specific.
- Check context and interpret impact of interventions and percentage improvement in net-score.
- Display output, which includes patient data, alerts, critiques and recommendations.
- Discard data older than the predefined time limit (currently set to two hours).
- Move contents of current state into previous state.
- Read in another set of data and repeat process.

At the beginning of each case run, the computer program prompts for the case identification number. Then the program asks for the type of output desired, with the choices being any one of detailed, summary, inclusive, assessment or pattern. After the first set of historical data has been processed, the program asks to see if it should continue processing the remaining data. If the answer is yes, then the program begins to process all the data until the end of file is reached; otherwise, the program asks for another case identification to be entered. The input sequence is shown in Figure 25. At present, the program has to be re-initialized prior to running each case; this is to delete schemas and values specific to the patient data created during the previous run. An example is the general drug-dosage tables, which need to be reset to their original values.



```
Please enter name of input file (Q to quit)?     "p9857310"
Do you want detail, summary, assessment, inclusive or pattern (D/S/A/I/P)?  I
Execution started at  (01-APR-93 1502)
Filename = /Hp-Sun.space/cvdata/p9857310
Do you want to loop automatically (y/n)?     y
```

Figure 25. The Studio layout of ARTIM, showing the input sequence of a typical run. The computer generated text is shown in regular text, whereas the user input text is highlighted in bold and italics. In this example, an inclusive run is requested on the stated patient case.

7.4.4. Types of Output

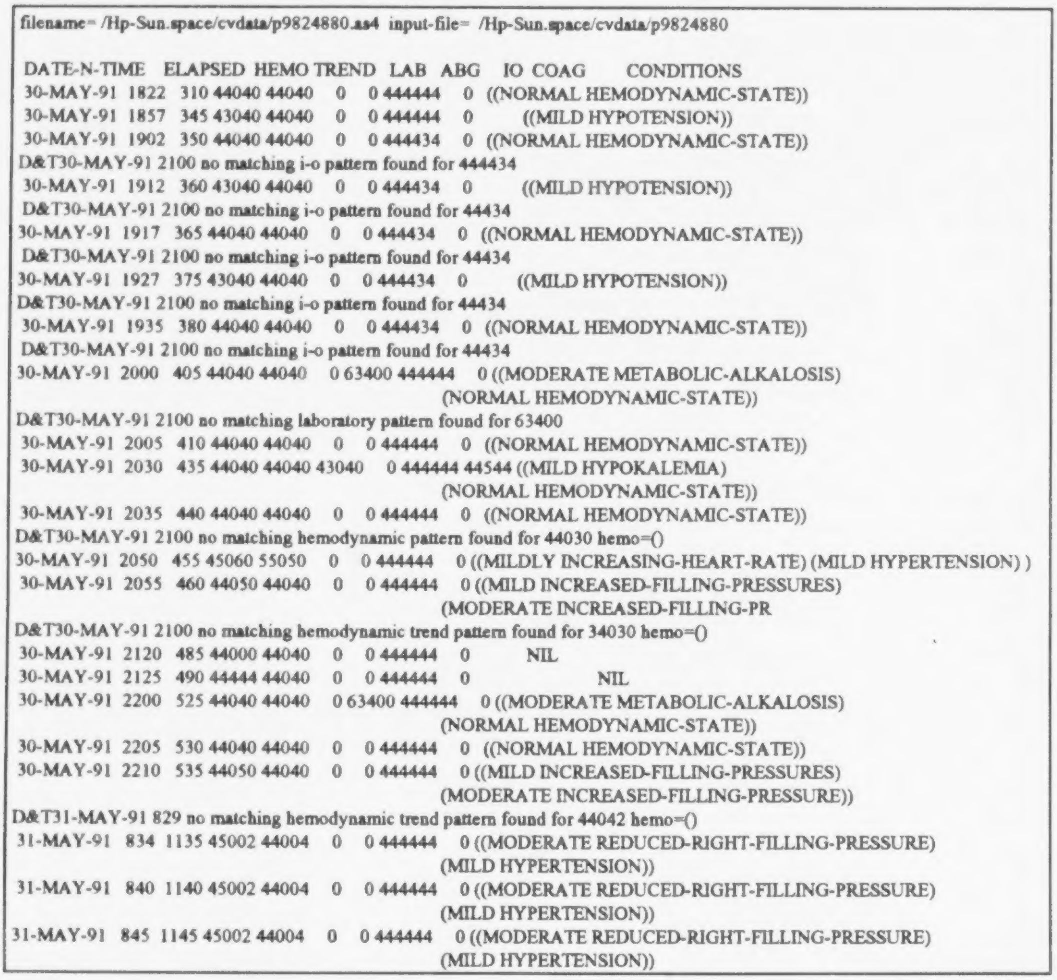
Four types of output are available – pattern analysis, detailed and summary reports, and dosage-response assessment. The nature of each output is described below.

Pattern analysis was done to analyze the critiqued learning cases; constructed patterns were matched against known patterns and conditions, patterns not in the knowledge base were displayed. The knowledge base would be updated and case rerun until all unknown patterns were classified. An example of the pattern analysis report is in Figure 26.

The detailed report provides a chronological printout of the patient data, instituted interventions, net-score values, recommended interventions, alerts and critiques, as well as the predicted and proposed patient conditions. The report, shown in Figure 27, allowed one to evaluate the consistencies of the recommendations and critiques.

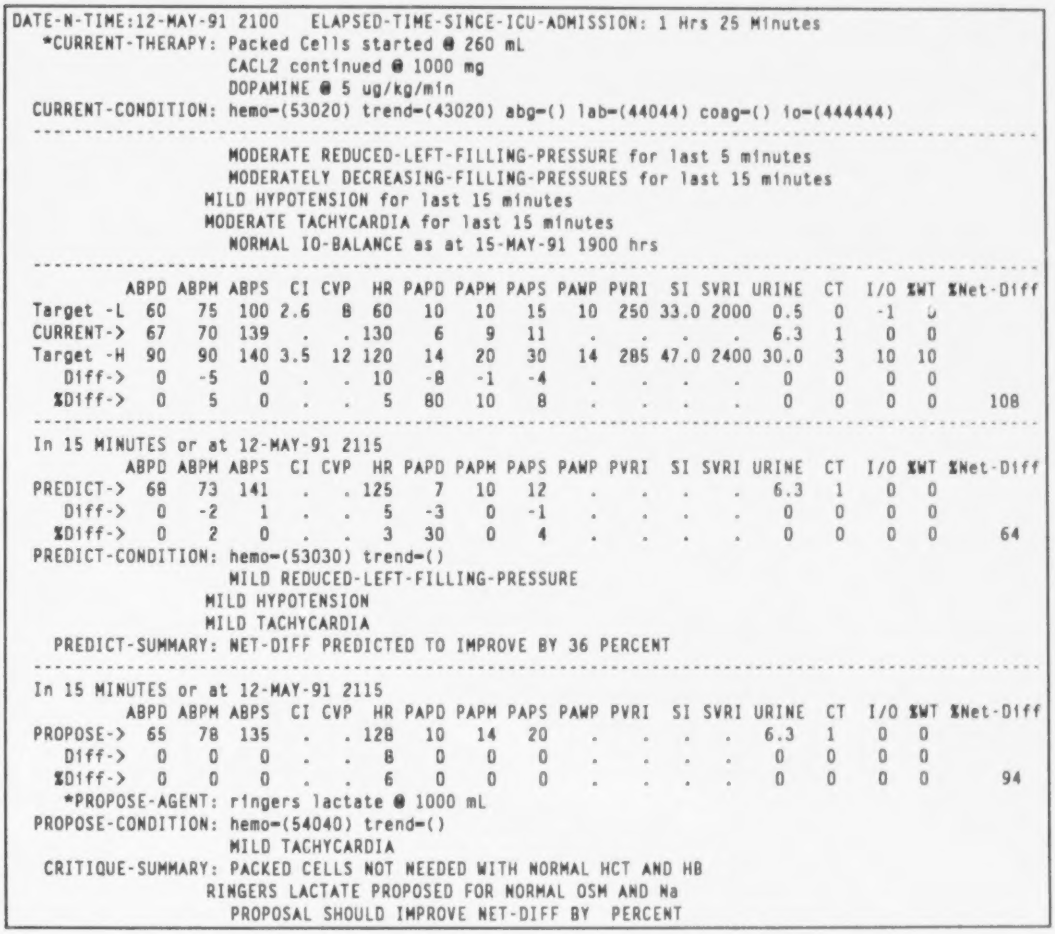
The summary report, shown in Figure 28, lists only the recommendations and critiques from each case and was used for tabulation during validation of the test cases.

The drug-dosage assessment report is a chronological listing of the computed drug-dosage responses for each intervention instituted. The assessment report, shown in Figure 29, allowed comparison of the expected and actual responses for each hemodynamic parameter from the drug-dosage effects.



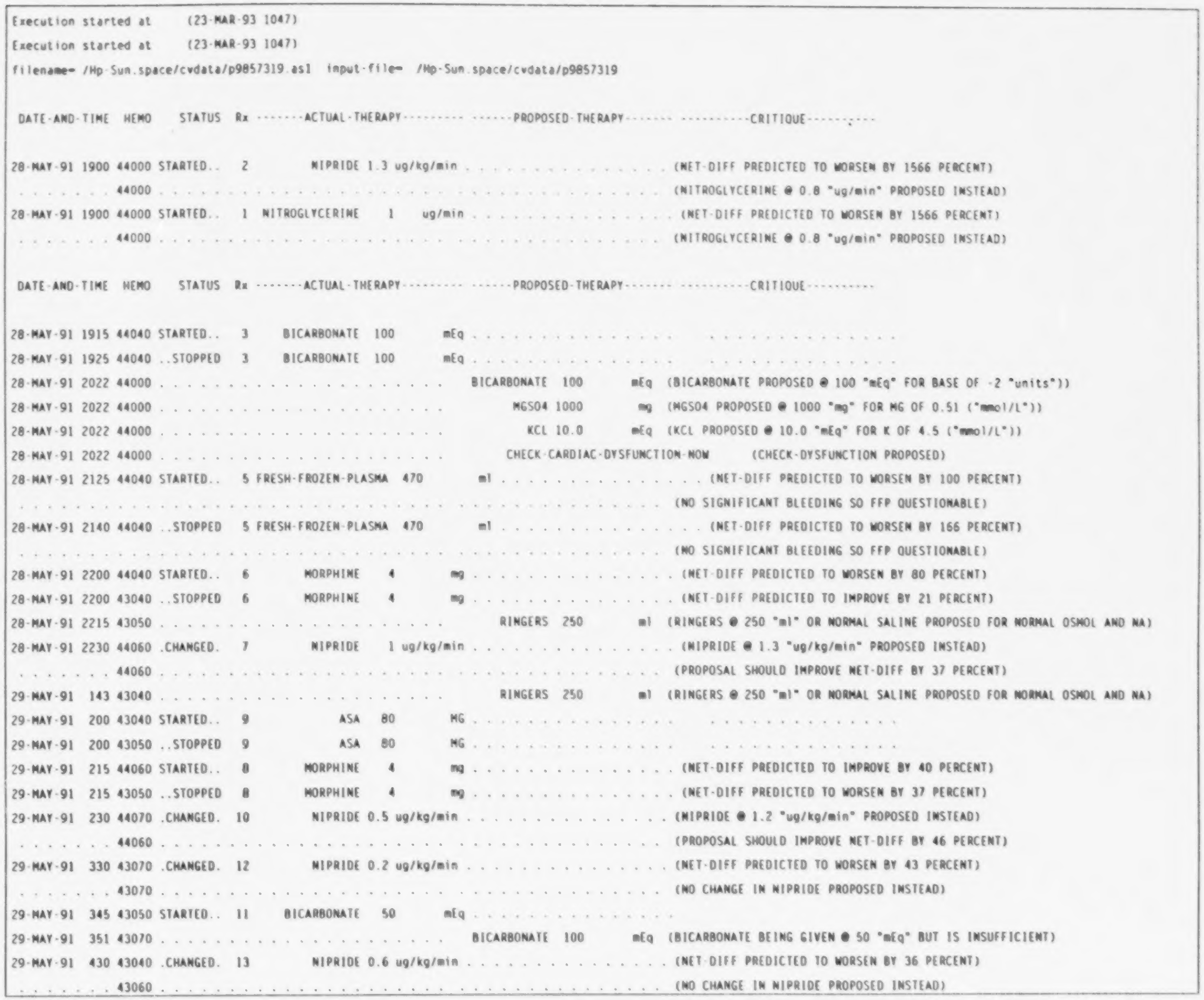
```
filename= /Hp-Sun.space/cvdata/p9824880.as4  input-file=  /Hp-Sun.space/cvdata/p9824880

 DATE-N-TIME   ELAPSED HEMO TREND  LAB  ABG   IO COAG      CONDITIONS
 30-MAY-91  1822   310 44040 44040    0    0 444444    0  ((NORMAL HEMODYNAMIC-STATE))
 30-MAY-91  1857   345 43040 44040    0    0 444444    0        ((MILD HYPOTENSION))
 30-MAY-91  1902   350 44040 44040    0    0 444434    0  ((NORMAL HEMODYNAMIC-STATE))
D&T30-MAY-91 2100 no matching i-o pattern found for 444434
 30-MAY-91  1912   360 43040 44040    0    0 444434    0        ((MILD HYPOTENSION))
 D&T30-MAY-91 2100 no matching i-o pattern found for 44434
30-MAY-91  1917   365 44040 44040    0    0 444434    0  ((NORMAL HEMODYNAMIC-STATE))
 D&T30-MAY-91 2100 no matching i-o pattern found for 44434
30-MAY-91  1927   375 43040 44040    0    0 444434    0        ((MILD HYPOTENSION))
D&T30-MAY-91 2100 no matching i-o pattern found for 44434
 30-MAY-91  1935   380 44040 44040    0    0 444434    0  ((NORMAL HEMODYNAMIC-STATE))
 D&T30-MAY-91 2100 no matching i-o pattern found for 44434
30-MAY-91  2000   405 44040 44040    0 63400 444444    0 ((MODERATE METABOLIC-ALKALOSIS)
                                                        (NORMAL HEMODYNAMIC-STATE))
D&T30-MAY-91 2100 no matching laboratory pattern found for 63400
 30-MAY-91  2005   410 44040 44040    0    0 444444    0  ((NORMAL HEMODYNAMIC-STATE))
 30-MAY-91  2030   435 44040 44040 43040    0 444444 44544 ((MILD HYPOKALEMIA)
                                                        (NORMAL HEMODYNAMIC-STATE))
 30-MAY-91  2035   440 44040 44040    0    0 444444    0  ((NORMAL HEMODYNAMIC-STATE))
D&T30-MAY-91 2100 no matching hemodynamic pattern found for 44030 hemo=()
30-MAY-91  2050   455 45060 55050    0    0 444444    0 ((MILDLY INCREASING-HEART-RATE) (MILD HYPERTENSION) )
 30-MAY-91  2055   460 44050 44040    0    0 444444    0 ((MILD INCREASED-FILLING-PRESSURES)
                                                        (MODERATE INCREASED-FILLING-PR
D&T30-MAY-91 2100 no matching hemodynamic trend pattern found for 34030 hemo=()
 30-MAY-91  2120   485 44000 44040    0    0 444444    0         NIL
 30-MAY-91  2125   490 44444 44040    0    0 444444    0                   NIL
 30-MAY-91  2200   525 44040 44040    0 63400 444444    0 ((MODERATE METABOLIC-ALKALOSIS)
                                                        (NORMAL HEMODYNAMIC-STATE))
 30-MAY-91  2205   530 44040 44040    0    0 444444    0  ((NORMAL HEMODYNAMIC-STATE))
 30-MAY-91  2210   535 44050 44040    0    0 444444    0 ((MILD INCREASED-FILLING-PRESSURES)
                                                        (MODERATE INCREASED-FILLING-PRESSURE))
D&T31-MAY-91 829 no matching hemodynamic trend pattern found for 44042 hemo=()
 31-MAY-91   834  1135 45002 44004    0    0 444444    0 ((MODERATE REDUCED-RIGHT-FILLING-PRESSURE)
                                                        (MILD HYPERTENSION))
 31-MAY-91   840  1140 45002 44004    0    0 444444    0 ((MODERATE REDUCED-RIGHT-FILLING-PRESSURE)
                                                        (MILD HYPERTENSION))
31-MAY-91   845  1145 45002 44004    0    0 444444    0 ((MODERATE REDUCED-RIGHT-FILLING-PRESSURE)
                                                        (MILD HYPERTENSION))
```

Figure 26. Typical output of a pattern-matching analysis.



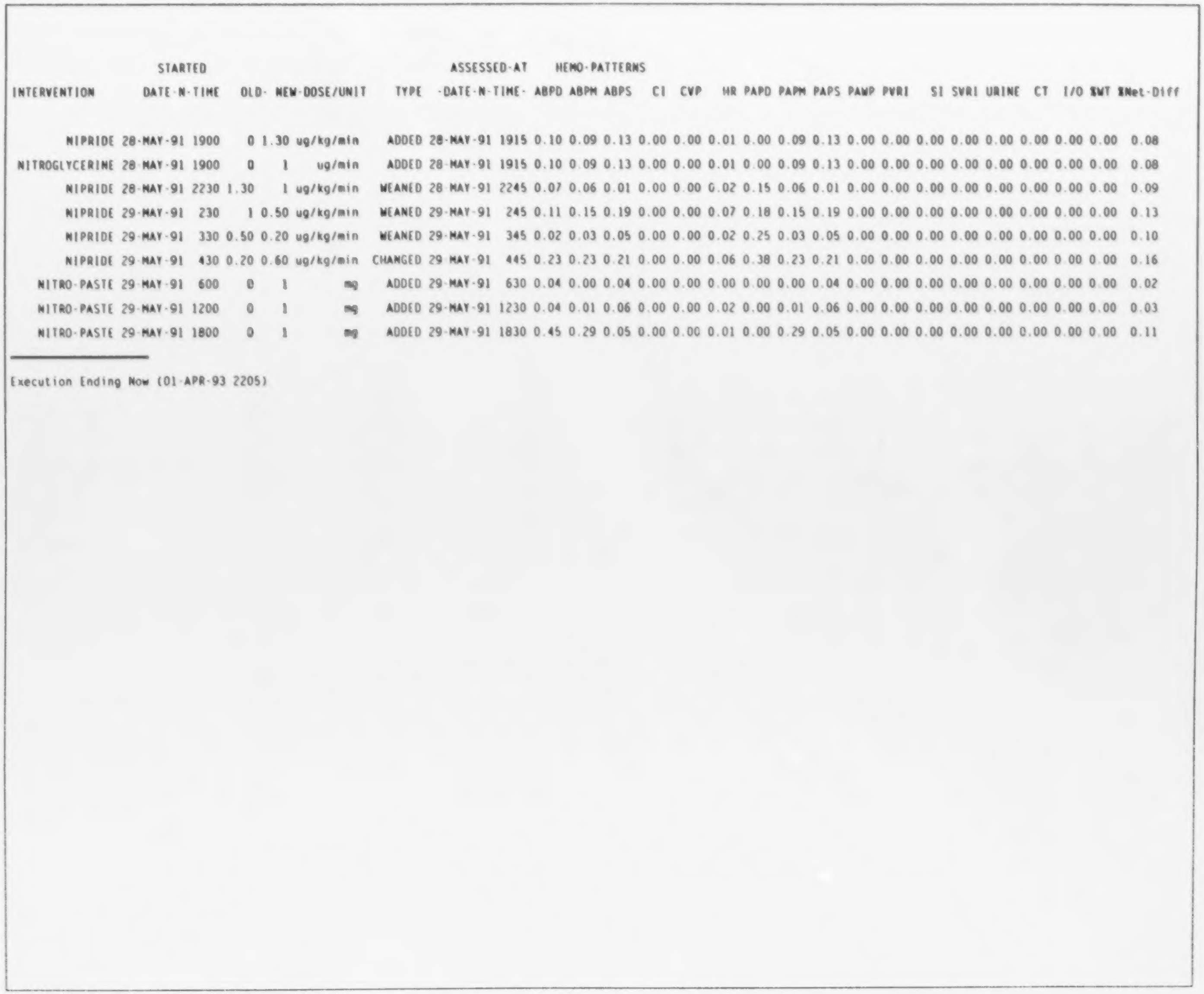
```
DATE-N-TIME:12-MAY-91 2100   ELAPSED-TIME-SINCE-ICU-ADMISSION: 1 Hrs 25 Minutes
   *CURRENT-THERAPY: Packed Cells started @ 260 mL
                     CACL2 continued @ 1000 mg
                     DOPAMINE @ 5 ug/kg/min
  CURRENT-CONDITION: hemo=(53020) trend=(43020) abg=() lab=(44044) coag=() io=(444444)
  ---------------------------------------------------------------------------------------
                     MODERATE REDUCED-LEFT-FILLING-PRESSURE for last 5 minutes
                     MODERATELY DECREASING-FILLING-PRESSURES for last 15 minutes
                   MILD HYPOTENSION for last 15 minutes
                   MODERATE TACHYCARDIA for last 15 minutes
                     NORMAL IO-BALANCE as at 15-MAY-91 1900 hrs
  ---------------------------------------------------------------------------------------
          ABPD ABPM ABPS  CI CVP  HR PAPD PAPM PAPS PAWP PVRI  SI SVRI URINE  CT  I/O %WT %Net-Diff
  Target -L  60   75  100 2.6   8  60   10   10   15   10  250 33.0 2000  0.5   0   -1   0
  CURRENT->  67   70  139   .   . 130    6    9   11    .    .    .    .  6.3   1    0   0
  Target -H  90   90  140 3.5  12 120   14   20   30   14  285 47.0 2400 30.0   3   10  10
     Diff->   0   -5    0   .   .  10   -8   -1   -4    .    .    .    .    0   0    0   0
    %Diff->   0    5    0   .   .   5   80   10    8    .    .    .    .    0   0    0   0      108
  ---------------------------------------------------------------------------------------
  In 15 MINUTES or at 12-MAY-91 2115
          ABPD ABPM ABPS  CI CVP  HR PAPD PAPM PAPS PAWP PVRI  SI SVRI URINE  CT  I/O %WT %Net-Diff
  PREDICT->  68   73  141   .   . 125    7   10   12    .    .    .    .  6.3   1    0   0
     Diff->   0   -2    1   .   .   5   -3    0   -1    .    .    .    .    0   0    0   0
    %Diff->   0    2    0   .   .   3   30    0    4    .    .    .    .    0   0    0   0       64
  PREDICT-CONDITION: hemo=(53030) trend=()
                     MILD REDUCED-LEFT-FILLING-PRESSURE
                   MILD HYPOTENSION
                   MILD TACHYCARDIA
    PREDICT-SUMMARY: NET-DIFF PREDICTED TO IMPROVE BY 36 PERCENT
  ---------------------------------------------------------------------------------------
  In 15 MINUTES or at 12-MAY-91 2115
          ABPD ABPM ABPS  CI CVP  HR PAPD PAPM PAPS PAWP PVRI  SI SVRI URINE  CT  I/O %WT %Net-Diff
  PROPOSE->  65   78  135   .   . 128   10   14   20    .    .    .    .  6.3   1    0   0
     Diff->   0    0    0   .   .   8    0    0    0    .    .    .    .    0   0    0   0
    %Diff->   0    0    0   .   .   6    0    0    0    .    .    .    .    0   0    0   0       94
     *PROPOSE-AGENT: ringers lactate @ 1000 mL
  PROPOSE-CONDITION: hemo=(54040) trend=()
                     MILD TACHYCARDIA
   CRITIQUE-SUMMARY: PACKED CELLS NOT NEEDED WITH NORMAL HCT AND HB
                   RINGERS LACTATE PROPOSED FOR NORMAL OSM AND Na
                     PROPOSAL SHOULD IMPROVE NET-DIFF BY  PERCENT
```

Figure 27. An example of the detailed report.



```
Execution started at     (23-MAR-93 1047)
Execution started at     (23-MAR-93 1047)
filename= /Hp-Sun.space/cvdata/p9857319.asl  input-file=  /Hp-Sun.space/cvdata/p9857319

 DATE-AND-TIME  HEMO    STATUS  Rx -------ACTUAL-THERAPY--------- ------PROPOSED-THERAPY------- ----------CRITIQUE-----.---

28-MAY-91 1900 44000 STARTED..   2         NIPRIDE 1.3 ug/kg/min . . . . . . . . . . . . . . . . . (NET-DIFF PREDICTED TO WORSEN BY 1566 PERCENT)
 . . . . . . . . 44000 . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . (NITROGLYCERINE @ 0.8 "ug/min" PROPOSED INSTEAD)
28-MAY-91 1900 44000 STARTED..   1  NITROGLYCERINE    1    ug/min . . . . . . . . . . . . . . . . . (NET-DIFF PREDICTED TO WORSEN BY 1566 PERCENT)
 . . . . . . . . 44000 . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . (NITROGLYCERINE @ 0.8 "ug/min" PROPOSED INSTEAD)

 DATE-AND-TIME  HEMO    STATUS  Rx -------ACTUAL-THERAPY--------- ------PROPOSED-THERAPY------- ----------CRITIQUE----------

28-MAY-91 1915 44040 STARTED..   3     BICARBONATE  100       mEq . . . . . . . . . . . . . . . .    . . . . . . . . . . . . . . .
28-MAY-91 1925 44040 ..STOPPED   3     BICARBONATE  100       mEq . . . . . . . . . . . . . . . .    . . . . . . . . . . . . . . .
28-MAY-91 2022 44000 . . . . . . . . . . . . . . . . . . . . . . .  BICARBONATE  100       mEq  (BICARBONATE PROPOSED @ 100 "mEq" FOR BASE OF -2 "units"))
28-MAY-91 2022 44000 . . . . . . . . . . . . . . . . . . . . . . .         MGSO4 1000        mg  (MGSO4 PROPOSED @ 1000 "mg" FOR MG OF 0.51 ("mmol/L"))
28-MAY-91 2022 44000 . . . . . . . . . . . . . . . . . . . . . . .           KCL 10.0       mEq  (KCL PROPOSED @ 10.0 "mEq" FOR K OF 4.5 ("mmol/L"))
28-MAY-91 2022 44000 . . . . . . . . . . . . . . . . . . . . . . .       CHECK-CARDIAC-DYSFUNCTION-NOW      (CHECK-DYSFUNCTION PROPOSED)
28-MAY-91 2125 44040 STARTED..   5 FRESH-FROZEN-PLASMA  470        ml . . . . . . . . . . . . . . . . . (NET-DIFF PREDICTED TO WORSEN BY 100 PERCENT)
 . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . (NO SIGNIFICANT BLEEDING SO FFP QUESTIONABLE)
28-MAY-91 2140 44040 ..STOPPED   5 FRESH-FROZEN-PLASMA  470        ml . . . . . . . . . . . . . . . . . (NET-DIFF PREDICTED TO WORSEN BY 166 PERCENT)
 . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . (NO SIGNIFICANT BLEEDING SO FFP QUESTIONABLE)
28-MAY-91 2200 44040 STARTED..   6        MORPHINE    4        mg . . . . . . . . . . . . . . . . . (NET-DIFF PREDICTED TO WORSEN BY 80 PERCENT)
28-MAY-91 2200 43040 ..STOPPED   6        MORPHINE    4        mg . . . . . . . . . . . . . . . . . (NET-DIFF PREDICTED TO IMPROVE BY 21 PERCENT)
28-MAY-91 2215 43050 . . . . . . . . . . . . . . . . . . . . . . .        RINGERS  250        ml  (RINGERS @ 250 "ml" OR NORMAL SALINE PROPOSED FOR NORMAL OSMOL AND NA)
28-MAY-91 2230 44060 .CHANGED.   7         NIPRIDE    1 ug/kg/min . . . . . . . . . . . . . . . . . (NIPRIDE @ 1.3 "ug/kg/min" PROPOSED INSTEAD)
 . . . . . . . . 44060 . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . (PROPOSAL SHOULD IMPROVE NET-DIFF BY 37 PERCENT)
29-MAY-91  143 43040 . . . . . . . . . . . . . . . . . . . . . . .        RINGERS  250        ml  (RINGERS @ 250 "ml" OR NORMAL SALINE PROPOSED FOR NORMAL OSMOL AND NA)
29-MAY-91  200 43040 STARTED..   9             ASA   80        MG . . . . . . . . . . . . . . . .    . . . . . . . . . . . . . . .
29-MAY-91  200 43050 ..STOPPED   9             ASA   80        MG . . . . . . . . . . . . . . . .    . . . . . . . . . . . . . . .
29-MAY-91  215 44060 STARTED..   8        MORPHINE    4        mg . . . . . . . . . . . . . . . . . (NET-DIFF PREDICTED TO IMPROVE BY 40 PERCENT)
29-MAY-91  215 43050 ..STOPPED   8        MORPHINE    4        mg . . . . . . . . . . . . . . . . . (NET-DIFF PREDICTED TO WORSEN BY 37 PERCENT)
29-MAY-91  230 44070 .CHANGED.  10         NIPRIDE 0.5 ug/kg/min . . . . . . . . . . . . . . . . . (NIPRIDE @ 1.2 "ug/kg/min" PROPOSED INSTEAD)
 . . . . . . . . 44060 . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . (PROPOSAL SHOULD IMPROVE NET-DIFF BY 46 PERCENT)
29-MAY-91  330 43070 .CHANGED.  12         NIPRIDE 0.2 ug/kg/min . . . . . . . . . . . . . . . . . (NET-DIFF PREDICTED TO WORSEN BY 43 PERCENT)
 . . . . . . . . 43070 . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . (NO CHANGE IN NIPRIDE PROPOSED INSTEAD)
29-MAY-91  345 43050 STARTED..  11     BICARBONATE   50       mEq . . . . . . . . . . . . . . . .
29-MAY-91  351 43070 . . . . . . . . . . . . . . . . . . . . . . .  BICARBONATE  100       mEq  (BICARBONATE BEING GIVEN @ 50 "mEq" BUT IS INSUFFICIENT)
29-MAY-91  430 43040 .CHANGED.  13         NIPRIDE 0.6 ug/kg/min . . . . . . . . . . . . . . . . . (NET-DIFF PREDICTED TO WORSEN BY 36 PERCENT)
 . . . . . . . . 43060 . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . (NO CHANGE IN NIPRIDE PROPOSED INSTEAD)
```

Figure 28. An example of the summary report.



```
                    STARTED                                      ASSESSED-AT     HEMO-PATTERNS
INTERVENTION      DATE-N-TIME   OLD- NEW-DOSE/UNIT     TYPE  -DATE-N-TIME- ABPD ABPM ABPS   CI  CVP   HR PAPD PAPM PAPS PAWP PVRI   SI SVRI URINE  CT  I/O %WT %Net-Diff


      NIPRIDE 28-MAY-91 1900    0 1.30 ug/kg/min   ADDED 28-MAY-91 1915 0.10 0.09 0.13 0.00 0.00 0.01 0.00 0.09 0.13 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00  0.08
NITROGLYCERINE 28-MAY-91 1900    0    1    ug/min   ADDED 28-MAY-91 1915 0.10 0.09 0.13 0.00 0.00 0.01 0.00 0.09 0.13 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00  0.08
      NIPRIDE 28-MAY-91 2230 1.30    1 ug/kg/min  WEANED 28-MAY-91 2245 0.07 0.06 0.01 0.00 0.00 0.02 0.15 0.06 0.01 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00  0.09
      NIPRIDE 29-MAY-91  230    1 0.50 ug/kg/min  WEANED 29-MAY-91  245 0.11 0.15 0.19 0.00 0.00 0.07 0.18 0.15 0.19 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00  0.13
      NIPRIDE 29-MAY-91  330 0.50 0.20 ug/kg/min  WEANED 29-MAY-91  345 0.02 0.03 0.05 0.00 0.00 0.02 0.25 0.03 0.05 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00  0.10
      NIPRIDE 29-MAY-91  430 0.20 0.60 ug/kg/min CHANGED 29-MAY-91  445 0.23 0.23 0.21 0.00 0.00 0.06 0.38 0.23 0.21 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00  0.16
   NITRO-PASTE 29-MAY-91  600    0    1        mg   ADDED 29-MAY-91  630 0.04 0.00 0.04 0.00 0.00 0.00 0.00 0.00 0.04 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00  0.02
   NITRO-PASTE 29-MAY-91 1200    0    1        mg   ADDED 29-MAY-91 1230 0.04 0.01 0.06 0.00 0.00 0.02 0.00 0.01 0.06 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00  0.03
   NITRO-PASTE 29-MAY-91 1800    0    1        mg   ADDED 29-MAY-91 1830 0.45 0.29 0.05 0.00 0.00 0.01 0.00 0.29 0.05 0.00 0.00 0.00 0.00 0.00 0.00 0.00 0.00  0.11
_______________

Execution Ending Now (01-APR-93 2205)
```

Figure 29. An example of an assessment report.

CHAPTER 8
PERFORMANCE VALIDATION

The methodology used to validate the performance of the prototype, and the results of the validation are described in this chapter.

8.1 Methodology

The validation approach, guidelines and methods used to validate the prototype are described in this section.

8.1.1 Approach

The essence of the validation was to apply the prototype to critiqued historical cases and compare results. Specifically, using the 13 historical cases reserved exclusively for testing, the interventions proposed by the prototype were compared with those of the expert critiques. A parallel comparison was made of the instituted interventions for the same cases against the expert critiques, and the performance of the prototype gauged against that of the staff.

While the comparison between prototype and staff had to be based on equal knowledge, it was necessary that the computer knew of interventions instituted, since these interventions influenced any subsequent decision-making. However, the time-sequential basis of the prototype precluded use of forward knowledge (e.g. the consequences of an intervention) and, at any instant, formulated the proposals before addressing the instituted interventions. The instituted interventions were then critiqued by the prototype, with the output for the time instant duly annotated.

The 13 test cases included 399 instituted interventions of types covered by the prototype. The expert critiques added 107 further interventional events, to make 506. Processing by prototype could, and did result in some proposal of interventions outside the 506 in nature and/or time; these, 44 in number, could not be evaluated properly, and were categorized as "questionable".

The relative performance of the proposed and instituted interventions against the expert critiques were tested with the statistical method, the chi-square. A summary of the validation approach is shown in Figure 30. Subjective comments by the author on the prototype design and findings were also included as part of the validation.

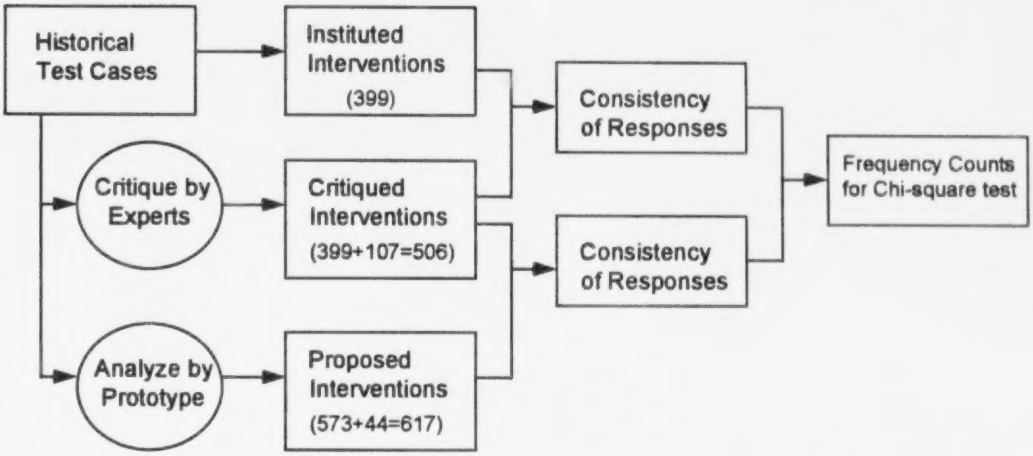

Historical Test Cases
Instituted Interventions (399)
Critique by Experts
Critiqued Interventions (399+107=506)
Analyze by Prototype
Proposed Interventions (573+44=617)
Consistency of Responses
Consistency of Responses
Frequency Counts for Chi-square test

Figure 30. Summary of the validation approach. Rectangles are data/knowledge; circles are processes.

While the concept of the research was to create a viable decision-support system running in real-time, the validation, of historical test cases, was run as a straight job on a computer workstation. The typical case, covering two days in the CVICU, took about five hours running exclusively on the SUN/ELC workstation (more on run-statistics in section 8.2.2).

Before running a test case, the initial target ranges defined by the expert who critiqued the case were manually entered as part of the historical patient data. The drug-dosage-table-update-flag was set in the configuration file so general drug-dose tables were automatically updated to become patient-specific during the run. When running a case, the "inclusive" option was specified to generate all three types of output at the same time, i.e. the detailed, summary and assessment reports. Any run-time errors (ranging from system errors, missing input data records, invalid input data, to system lock-ups) that occurred were also recorded.

A 24-hour limit was placed on each case run; any run not completed by the end of the 24-hour period was manually aborted. This was based on experience from developing the prototype that any case that took longer than 24 hours to run had probably run into a memory-swapping deadlock, requiring the ARTIM program to be aborted. Occasionally, the program aborted due to invalid and/or missing input data, absent therapeutic agent codes and/or invalid dosages. These errors were rectified and the cases re-run.

At the end of each run, the total number of rules fired, the total time it took to execute the program, and the number of rules fired per second were recorded from the screen. The instituted and proposed interventions from each test case were tabulated using a Lotus spreadsheet and compared with the expert critiques based on the predefined validation guidelines (see next section). Detailed tracings of the reasoning steps were performed to explain any differences noted.

8.1.2 Validation Guidelines

Five intervention categories were defined based on the types of interventions. The names of the categories and the types of interventions included for validation are:

Inotrope

- increasing and weaning of dosages for agents such as dopamine, dobutamine and inocore.

Vasoactive

- increasing and weaning of dosages for agents such as norepinephrine and nipride.

Fluid

- crystalloids, being normal saline, ringers lactate and D5W.
- colloids, being 5% and 25% albumin.

Bleeding

- therapeutic agents for bleeding, being packed cells, fresh-frozen plasma, platelets, cryoprecipitate, protamine and amicar.

Electrolyte

- Electrolyte-replacements, such as $MgSO_4$, $NaHCO_3$, KCl and $CaCl_2$.

The appropriateness of each intervention was rated in one of four validation categories related to the expert critiques: consistent, equivalent, questionable, and inconsistent, to which no-response was added for the absence of an intervention when the expert had suggested one. The five validation categories are defined as follows:

Consistent

where the intervention occurred within an hour of one suggested by the expert that was the same drug with the same direction of change in its dosage. For instance, if the expert had suggested increased dopamine, and if such an intervention was instituted or proposed, then it would be a consistent response.

Equivalent

where the intervention occurred within an hour of one suggested by the expert among a list of alternatives. For instance, if the expert had expressed an indifference to the use of colloid or crystalloid, and if either agent was instituted or proposed, then it would be an equivalent response.

Questionable

where the expert had expressed reservations about the appropriateness of an intervention under the circumstance, or required further information before reaching a conclusion.

Inconsistent

where the intervention occurred within an hour of one deemed inconsistent by the expert based on the protocols. For example, if the expert had indicated it was improper to raise the level of nitroglycerine given the patient's condition, and if an increase in nitroglycerine was instituted or proposed, then it would be an inconsistent response.

No-response

where the expert had suggested an intervention, but no such intervention choice was instituted or proposed within the hour. For example, if the expert had recommended ringers lactate to be given, and there was none instituted or proposed, it is considered a no-response.

Also included in the validation were other categories of responses unique to the prototype, which are:

- the number of diagnostic tests proposed, being check CVP/ART lines, hypertension, dysrhythmia and dysfunction; confirm CVP/ART lines; perform modified Trendelenburg test.
- the number of programming errors, including software errors that caused the program to abort, or errors detected in the output. Examples included division-by-zero, attempts to access deleted schemas, duplicate recommendations and memory-swapping deadlocks.
- the number of data entry errors on the test cases, including wrong agent codes, dosage levels, dates and/or times and missing data.
- the number of unclassified physiologic patterns.

In tallying the categorized responses, some additional guidelines were provided to ensure realistic counts dealing mainly with the logistics of the validation process, they are:

- Each time there was an instituted or proposed change to an intervention, such as an addition, a change in dosage, or a discontinuation, the intervention had to be validated against the expert critiques and tallied under one of the five validation categories.
- The recommendation cycle was arbitrarily set to one hour. This applied to situations where the same clinical condition persisted for more than one hour, and the prototype had already generated the appropriate recommendation earlier. If the same recommendation appeared again, it would be counted separately only if the time interval between the two recommendations were at least one hour in duration. The reason for this rule was that these represented continuous quality improvement opportunities that could have been exploited.
- For any unclassified patterns that were in the output, regardless of the number of times a pattern occurred within and between the cases, it would only be counted once. Thus, if the hemodynamic status pattern 43010 appeared 65 times from the 13 test cases, it would still be counted as one unclassified status pattern.

- The prototype was not to be modified during the validation process, despite any software errors noted when running the test cases. This was to avoid changing the behavior of the prototype by fixing the errors, which could render the results incomparable.

8.1.3 Validation Methods

The chi-square statistic, χ^2, was the validation method used to analyze the frequency counts of the categorized responses. Specifically, χ^2 tests for the homogeneity of the proportions of responses within each category from the prototype and the staff against the expert critiques. If the responses from the prototype and the staff were comparable in quality, the proportions would be similar for all categories; hence, no significant differences would be expected.

The χ^2 method consists of defining the null-hypothesis, calculating the expected value of each cell within the contingency table under each category, deriving the χ^2 statistic, obtaining the probability value from the χ^2 distribution table, and deciding whether to reject the hypothesis or not. In our study, the null-hypothesis was that the consistency of interventions proposed by the prototype and those instituted by the staff were no different based on the expert critiques. The hypothesis can be stated as follows:

Ho : the proportions of consistent interventions proposed by the prototype and those instituted by the staff were equal.

Ha: the proportions of consistent interventions proposed by the prototype and those instituted by the staff were unequal

and the equation for calculating the chi-square is

$$\chi^2 = \Sigma [(O - E)^2 / E]$$

where O is the observed frequency and E is the expected frequency. The level of significance used was 0.01 since multiple comparisons were expected.

A qualitative method was also included as part of the validation. The method involved subjective judgments on the prototype's design and performance using the structure-process-outcome model suggested by Wyatt (1990). The judgments consisted of critiques on the conceptual and structural design of the prototype, the reasoning capability in terms of consistency and efficiency, and the overall accuracy and completeness of the test results.

8.2 Validation Results

The validation results are presented in this section. The results consist of the characteristics of the historical cases, size of the prototype, run-time characteristics, test results, detailed findings and subjective judgments.

8.2.1 Characteristics of Historical Cases

The characteristics of the historical learning and test cases were summarized and shown in Table 20. The cases were compared based on sex, LOS (in days) and the type of pressure monitoring used. From the table, it can be observed that: there were more male cases than female in both groups; median LOS was 2 days for both groups; PA-catheter was more frequently used than CVP-only in both groups.

	SEX		LOS (days)				TYPE OF MONITORING	
CASE	Male	Female	1	2	3	4	CVP-only	PA-catheter
Learning	9	4	4	6	2	1	4	9
Test	10	3	3	6	3	1	5	8

Table 20. Characteristics of the historical cases.

8.2.2 Size of the Prototype

The size of the prototype was judged by the number of slots, facts, schemas, rules and functions defined, known as the entities. However, no guidelines had been provided initially to standardize the entities in terms of their size and coding style. As a result, the entities in the prototype varied from a few to over 100 lines of ARTIM code. Thus, the statistics represented only an indirect estimate of the size and complexity of the prototype. The type and count of the ARTIM entities are shown in Tables 21 (a) and (b). The "total" column in the tables contains the total count of an entity type, which can be as a rule, function, fact, variable, slot or schema.

TYPE	DESCRIPTION	COUNT	TOTAL
Rule	Input	20	193
	Interpret	30	
	Manage	4	
	Compute	7	
	Compare	13	
	Propose - general	39	
	Propose - fluids protocols	10	
	Propose - bleeding protocols	5	
	Propose - reverse protocols	21	
	Propose - other protocols	8	
	Interact	16	
	Prepare	18	
	Phase-Control	2	

Table 21 (a). The type and count of the ARTIM entities defined in the prototype.

TYPE	DESCRIPTION	COUNT	TOTAL
Function	Both ARTIM- and user-defined functions	161	161
Global Variable	All global variables	95	95
Fact	Defined and asserted facts	0	0
Slot	Multi-valued slots with/without inheritance	199	254
	Single-valued slots	55	
Schema	Patient-specific schemas	55	1,002
	Control schemas	5	
	Conditions	120	
	Drug-dosage levels	238	
	Diagnostic tests	46	
	Abnormality-hemo	266	
	Abnormality-hemo-trend	50	
	Abnormality-coag	24	
	Abnormality-io	28	
	Abnormality-lab	60	
	Abnormality-abg	33	
	Abnormality-coag-io	5	
	Therapeutic agents	72	

Table 21 (b). The type and count of the ARTIM entities defined in the prototype.

8.2.3 Run-Time Characteristics

The run-time characteristics were: the minimum, maximum and average figures on the total run-time, total rules fired and number of rules fired per second; the number of cases aborted in 24 hours; the number of software and data errors; the number of missing agents; the number of unknown physiologic patterns. The characteristics are tabulated in Tables 22 (a) and (b). The total run-time shows it took only 4.8 hours on average to run each of the seven test cases, firing close to 48,646 rules per run; but the other six cases had to be aborted after 24 hours. The software errors included duplicate and missing therapy recommendations. The data errors were due to wrong drug codes and dosage levels in the patient historical data files. Twelve missing agents had to be added to the knowledge base, with most being miscellaneous medications such as vasotec.

	# CASES	MINIMUM	MAXIMUM	AVERAGE	TOTAL
Total Run-Time in Hours	7	0.7	18.6	4.8	
Total Rules Fired	7	29,715	60,059	48,646	
Rules Fired per Second	7	0.9	12.8	6.6	
Aborted in 24 Hours	6				6
Program Error	13				15
Data Error	13				40
Missing Agent	13				12

Table 22 (a). Run-time statistics of the 13 test cases.

HEMO-STATUS	HEMO-TREND	COAG	IO	LAB	ABG
45	19	10	3	18	6

Table 22 (b). The total number of unknown physiologic patterns reported. Note that each unique unknown pattern was counted once only, regardless of how many times that pattern appeared.

8.2.4 Test Results

The frequency of the interventions proposed by the prototype and those instituted by the staff were tabulated by the intervention types under the five validation categories. Inotropes and vasoactive agents were further subdivided as increasing, weaning and no-change in dosage. Other responses counted were the categories unique to the prototype, such as check-lines and check-dysrhythmia, as well as run-time statistics and unknown patterns. An example of the tabulated results from a test case is shown in Table 23.

		PROTOTYPE					STAFF				
		C	E	I	Q	N	C	E	I	Q	N
Crystalloid		5				2	1				6
Albumin			2					3			
Protamine		1							1		
Amicar		1					1				
Dopamine	↑	4									4
	↓	2					2		4		
	N/C										
Nitroglycerine	↑										
	↓	1				2	1				2
	N/C										
Nipride	↑	1		1			2				
	↓	5					3				
	N/C										
K		1				4	4		1		
Mg						1			1	1	
Ca		1				1	2				
HCO_3		1				1	2				
Confirm lines		3									
Check dysfunction		1									
Check hypertension		1									
Program error		4									
Data error		3									
Hemo pattern		2									
IO pattern		1									
Coag pattern		1									
Lab pattern		1									

Table 23. An example of the tabulated results for one test case. Legend: C-consistent; E-equivalent; I-inconsistent; Q-questionable; N-no response; ↑ -increased; ↓ -weaned; N/C-nochange.

Once the individual frequency counts were tabulated, they were aggregated over all 13 test cases by the five intervention categories under the five validation categories. The aggregated counts of the interventions proposed by the prototype and those instituted by the staff are tabulated separately and shown in Tables 24 (a) and (b). Since some of the cells within the two aggregate tables contained zero counts, these empty cells had to be merged with others before the chi-square test could be performed. This is because chi-square requires a minimum frequency count of five in each cell (Harnett 1982). To eliminate zero counts, the five validation categories were collapsed into two: consistent and inconsistent, consistent including consistent and equivalent, inconsistent including inconsistent, questionable and no-response.

	Consistent	Equivalent	Inconsistent	Questionable	No-Response
Inotrope	57	0	19	2	34
Vasoactive	97	2	40	28	33
Fluid	44	23	4	11	12
Bleeding	39	0	0	3	2
Electrolyte	84	0	2	0	82
Total	321	25	65	44	163

Tables 24 (a). Aggregated frequency counts of the interventions, as proposed by the prototype.

	Consistent	Equivalent	Inconsistent	Questionable	No-Response
Inotrope	53	6	19	0	33
Vasoactive	69	10	16	12	31
Fluid	3	23	5	2	33
Bleeding	18	0	13	6	1
Electrolyte	115	0	17	12	9
Total	258	39	70	32	107

Tables 24 (b). Aggregated frequency counts of the interventions, as instituted by the staff.

The two aggregate tables were merged into one summary table by pairing the responses from the prototype and the staff by intervention category then by validation category, to form five intervention groups. A PC-based statistical software package called Numerical Cruncher Statistical System (NCSS) was used to compute the χ^2 statistic for each group. The χ^2 values obtained were compared against the χ^2 distribution table at a significance level of 0.01 with one degree of freedom, which has a critical value of 6.63. The frequency counts of each intervention group, the χ^2 values and the corresponding p-values are shown in Table 25.

The results show the fluid, bleeding and electrolyte intervention groups had χ^2 values exceeding 6.63 and significant p-values ($p \leq 0.0001$). For these three groups, one would reject the null-hypothesis that the proportions of consistent and inconsistent interventions were equal between the prototype and the staff. On the other hand, the inotrope and vasoactive groups had χ^2 values of 0.108 and 1.966, respectively, and insignificant p-values ($p > 0.01$). The null-hypothesis was accepted in that, for the inotropic and vasoactive agent interventions, the proportions of consistent and inconsistent interventions were equal between the prototype and the staff.

GROUP	RESPONSE	PROTOTYPE	STAFF	χ^2	P-VALUE
Inotrope	Consistent	57 (50.9%)	59 (53.2%)	0.108	0.743
	Inconsistent	55 (49.1%)	52 (46.8%)		
Vasoactive	Consistent	99 (49.5%)	79 (57.2%)	1.966	0.161
	Inconsistent	101 (50.5%)	59 (42.8%)		
Fluid	Consistent	67 (71.3%)	26 (39.4%)	16.19	0.0001
	Inconsistent	27 (28.7%)	40 (60.6%)		
Bleeding	Consistent	39 (88.6%)	18 (47.4%)	16.385	0.0001
	Inconsistent	5 (11.4%)	20 (52.6%)		
Electrolyte	Consistent	84 (50%)	115 (75.2%)	21.52	0.0001
	Inconsistent	84 (50%)	38 (24.8%)		

Table 25. A summary table containing the five intervention groups, showing the χ^2 and p-value for each group. The percentage underneath each aggregate count is the percentage of consistent and inconsistent responses for each group.

The summary table shows that, for the fluid group, the percentage of consistent responses from the prototype was 71.3%, versus 39.4% from the staff. For bleeding, the percentage of consistent responses from the prototype was 88.6%, versus 47.4% from the staff. Based on the significant p-values (p<0.0001) and the higher percentage of consistent interventions for these two groups, one can conclude that the prototype performed significantly better than the staff in recommending therapies for fluid replacement and bleeding. The opposite is true with electrolyte-replacement therapies, which were only 50% consistent for the prototype, versus 75.2% for the staff (p<0.0001). For the inotrope group, the percentage of consistent interventions was 50.9% for the prototype, 53.2% for the staff; for the vasoactive group, the percentages were 49.5% and 57.2% for the prototype and staff, respectively. The p-values for both groups were not significant, suggesting the prototype performed no better than the staff in providing inotropic and vasoactive therapies.

8.2.5 Detailed Findings

A detailed breakdown of the fluid group by intervention type and validation category is shown in Table 26. From the table, it can be observed that the prototype correctly proposed the use of crystalloid for 44 times, versus 3 times by the staff. Although only 63% of the prototype's proposed use of crystalloid were consistent, this percentage was much higher than the 8% from the staff. In fact, crystalloids were not instituted by the staff 89% of the time when recommended by the expert.

For albumin, the prototype recommended the use of an equivalent crystalloid agent 23 times, which concurred entirely with the expert. These findings suggest the prototype was able to avoid the use of albumin by recommending crystalloid, which would have been equally acceptable. This has a cost-saving implication, since a 250 mL bottle of 5% albumin costs $100, while 1 litre of crystalloid, such as ringers, costs only $1.25. From the 13 test cases, a potential saving of over $2,500 could have been realized if crystalloid therapy had been used instead of albumin.

Fluid	Consistent	Equivalent	Inconsistent	Questionable	No-Response
Crystalloid					
- prototype	44 (63%)		3 (4%)	10 (15%)	12 (18%)
- staff	3 (8%)		1 (3%)		33 (89%)
Albumin					
- prototype		23 (92%)	1 (4%)	1 (4%)	
- staff		23 (79%)	4 (14%)	2 (7%)	

Table 26. A detailed breakdown of the fluid group by intervention type and validation category. The percentage to the right of the frequency count is the row percentage.

A detailed breakdown of the bleeding intervention group is shown in Table 27. The table shows 89% of the proposed interventions by the prototype were consistent, versus 47% by the staff. In particular, 87% of the proposed interventions regarding packed cells were consistent, as opposed to 59% by the staff. Considering the relatively high frequency of usage for packed cells in the CVICU to treat active bleeding (over 40%), it would appear the prototype could improve the cost-effective use of packed cells significantly.

AS PROPOSED BY THE PROTOTYPE

Bleeding	Consistent	Equivalent	Inconsistent	Questionable	No-Response
FFP	5 (13%) (100%)				
Protamine	3 (7%) (100%)				
Amicar	5 (13%) (100%)				
Packed Cells	20 (51%) (87%)			2 (67%) (9%)	1 (50%) (4%)
Auto-trans	1 (3%) (50%)				1 (50%) (50%)
Vitamin-K1	3 (8%) (100%)				
Cryo	2 (5%) (67%)			1 (33%) (33%)	
Total	39 (100%) (89%)			3 (100%) (7%)	2 (100%) (4%)

AS INSTITUTED BY THE STAFF

Bleeding	Consistent	Equivalent	Inconsistent	Questionable	No-Response
FFP	1 (6%) (25%)		1 (8%) (25%)	2 (33%) (50%)	
Protamine			3 (23%) (100%)		
Amicar	5 (28%) (83%)			1 (17%) (17%)	
Packed Cells	10 (55%) (59%)		5 (38%) (29%)	1 (17%) (6%)	1 (100%) (6%)
Auto-trans	2 (11%) (100%)				
Vitamin-K1			2 (15%) (67%)	1 (16%) (33%)	
Cryo			2 (15%) (67%)	1 (17%) (33%)	
Total	18 (100%) (47%)		13 (100%) (34%)	6 (100%) (16%)	1 (100%) (3%)

Table 27. A detailed breakdown of the bleeding intervention group. The percentage to the right of the frequency count in each cell is the column percentage; the percentage underneath is the row percentage. Legend: FFP - fresh-frozen plasma; Cryo - cryoprecipitates.

While 75% of the fresh-frozen plasma (FFP) interventions instituted by the staff were considered inconsistent or questionable, the prototype was 100% consistent with the expert critiques in proposing when FFP was needed. The use of protamine and cryoprecipitate by the staff was the least satisfactory, being 100% inconsistent. While the prototype was 100% correct in proposing the use of protamine, it was only 67% consistent with cryoprecipitate. Closer examination of the program logic revealed that the errors were due to the unavailability of laboratory results and software errors in handling the CT results. These findings suggest current practice on treating active bleeding is not consistent.

The prototype performed no better than the staff in the use of inotropes and vasoactive agents. Detailed breakdowns of the inotrope and vasoactive intervention groups are shown in Tables 28 and 29, respectively. For the inotrope group, the respective frequencies across all validation categories between the prototype and staff were almost identical, suggesting the prototype made the same proportions of consistent and inconsistent responses as the staff. For the vasoactive group, the prototype had 97 responses that were consistent, versus only 69 by the staff. However, the prototype also had 68 responses that were inconsistent or questionable, versus only 28 by the staff. These observations suggest the prototype was more aggressive in critiquing vasoactive therapies, but it did so at a higher risk of proposing inconsistent therapies. Tracings of the program logic revealed the improper encoding of the net-scoring/ranking algorithms and the comparison of intervention choices against the patient's context were likely the sources of the errors.

A detailed breakdown of the electrolyte intervention group is shown in Table 30. The table shows that for the prototype, only 50% of the responses were consistent, versus 75% for the staff. The prototype also had 49% no-responses, versus only 6% for the staff. Tracings of the program logic revealed the main source of errors to be due to unclassified laboratory patterns. A few were caused by a software error in not being able to obtain the proper laboratory results from the appropriate schemas.

AS PROPOSED BY THE PROTOTYPE

INOTROPE	Consistent	Equivalent	Inconsistent	Questionable	No-Response
- Up	13 (23%) (42%)		2 (11%) (6%)		16 (47%) (52%)
- wean	36 (63%) (54%)		13 (68%) (19%)	2 (100%) (3%)	16 (47%) (24%)
- same	8 (14%) (57%)		4 (21%) (29%)		2 (6%) (14%)
Total	57 (100%) (51%)		19 (100%) (17%)	2 (100%) (2%)	34 (100%) (30%)

AS INSTITUTED BY THE STAFF

INOTROPE	Consistent	Equivalent	Inconsistent	Questionable	No-Response
- Start/up	9 (17%) (26%)		9 (47%) (26%)		16 (48%) (48%)
- wean	44 (83%) (59%)	6 (100%) (8%)	10 (53%) (13%)		15 (46%) (20%)
- same					2 (6%) (100%)
Total	53 (100%) (48%)	6 (100%) (5%)	19 (100%) (17%)		33 (100%) (30%)

Table 28. A detailed breakdown of the inotrope intervention group. The percentage to the right of the frequency count in each cell is the column percentage; the percentage underneath each count is the row percentage.

AS PROPOSED BY THE PROTOTYPE

VASO	Consistent	Equivalent	Inconsistent	Questionable	No-Response
- Up	20 (21%) (44%)	1 (50%) (2%)	16 (40%) (36%)	2 (7%) (4%)	6 (18%) (14%)
- wean	74 (76%) (54%)		16 (40%) (11%)	21 (75%) (15%)	27 (82%) (20%)
- same	3 (3%) (18%)	1 (50%) (6%)	8 (20%) (47%)	5 (18%) (29%)	
Total	97 (100%) (49%)	2 (100%) (1%)	40 (100%) (20%)	28 (100%) (14%)	33 (100%) (16%)

AS INSTITUTED BY THE STAFF

VASO	Consistent	Equivalent	Inconsistent	Questionable	No-Response
- start/up	23 (34%) (56%)	5 (50%) (12%)	5 (31%) (12%)	2 (16%) (5%)	6 (19%) (15%)
- wean	43 (62%) (52%)	5 (50%) (6%)	5 (31%) (6%)	5 (42%) (6%)	25 (81%) (30%)
- same	3 (4%) (21%)		6 (38%) (43%)	5 (42%) (36%)	
Total	69 (100%) (50%)	10 (100%) (7%)	16 (100%) (12%)	12 (100%) (9%)	31 (100%) (22%)

Table 29. A detailed breakdown of the vasoactive intervention group. The percentage shown to the right of the frequency count in each cell is the column percentage; the percentage underneath each count is the row percentage.

AS PROPOSED BY THE PROTOTYPE

ELECTRO	Consistent	Equivalent	Inconsistent	Questionable	No-Response
K	53 (63%) (52%)				48 (59%) (48%)
Mg	6 (7%) (29%)				15 (18%) (71%)
Ca	2 (2%) (17%)				10 (12%) (83%)
HCO_3	23 (28%) (68%)		2 (100%) (6%)		9 (11%) (26%)
Total	84 (100%) (50%)		2 (100%) (1%)		82 (100%) (49%)

AS INSTITUTED BY THE STAFF

ELECTRO	Consistent	Equivalent	Inconsistent	Questionable	No-Response
K	74 (64%) (89%)		6 (35%) (7%)	1 (8%) (1%)	2 (23%) (3%)
Mg	8 (7%) (32%)		7 (41%) (28%)	6 (50%) (25%)	4 (44%) (15%)
Ca	9 (8%) (50%)		2 (12%) (11%)	4 (34%) (22%)	3 (33%) (17%)
HCO_3	24 (21%) (89%)		2 (12%) (7%)	1 (8%) (4%)	
Total	115 (100%) (75%)		17 (100%) (11%)	12 (100%) (8%)	9 (100%) (6%)

Table 30. A detailed breakdown of the electrolyte intervention group. The percentage to the right of the frequency count in each cell is the column percentage; the percentage underneath is the row percentage.

The frequencies of the diagnostic interventions produced by the prototype are shown in Table 31. The interventions consisted of CVP/ART lines to be checked and confirmed, requests to perform the modified Trendelenburg positioning, and checking for problems when no protocol was available (i.e. hypertension, dysrhythmia and cardiac dysfunction). The 13 test cases had included nursing notes that mentioned 25 occasions where the transducers were "re-zeroed" (not shown in table). The table shows 32 occasions where the prototype had proposed to check CVP/ART lines for missing data, and 86 occasions where the data had appeared spurious, requiring confirmation by the staff. The 127 proposed interventions to check for problems would have alerted the staff, even in the absence of formalized protocols in the system. All of these diagnostic interventions represented clinical quality improvement opportunities, since they would prompt immediate attention of the staff.

Check lines	Confirm lines	Hypertension	Dysfunction	Dysrhythmia	Trendelenbg
32	86	65	49	13	25

Table 31. Frequencies of diagnostic intervention produced by the prototype.

There were 12 occasions where the experts had indicated an opportunity to redefine the target range for certain hemodynamic parameters, and another 9 occasions where cardiac output assessment should have been done. Neither the staff nor the prototype had offered such interventions. The prototype also failed to produce any recommendations to wean the patient from inotropic or vasoactive therapies. However, the hemodynamic data from those test cases where the prototype had failed to respond were not examined to determine the cause, due to the extensive efforts required.

8.2.6 Subjective Judgments

Subjective judgments of the conceptual and structural design of the prototype, the reasoning capability in terms of consistency and efficiency, and the overall accuracy and completeness of the test results are summarized below.

Conceptual and Structural Design

The conceptual framework and the knowledge representation scheme used were considered appropriate because one was able to adequately express the relevant cardiovascular and therapeutic management knowledge (Ringland 1987). The use of schemas and rules allowed the resulting knowledge components to be defined at a granular level suitable for solving the problem, i.e. distinguishing the clinical conditions and providing the appropriate therapeutic management recommendations. The primitives consisted of physiologic parameters and patterns, condition names, patient states, intervention strategies, therapeutic agents and dosage levels, etc. which are the nomenclatures commonly used in the CVICU environment.

The sources of expert knowledge were based on textbooks, experience of two expert physicians and review of 13 historical CVICU cases. It appeared the knowledge to diagnose and manage hypovolemic hypotension was extracted successfully, as was demonstrated by the performance of the prototype. The only drawback was the inherent uncertainty with the general drug-dosage response tables and the net-scoring/ranking heuristics, which could have been further verified with multiple experts.

However, the structure of the prototype was inadequate due to limitations in the programming language used. Specifically, the ARTIM software tool lacked the appropriate database access functions, which had forced the structural design of the prototype to be entirely schema-driven, using external files only for input data processing. While ARTIM was flexible as a list programming language, it lacked even such basic functions as date and time handling, which resulted in extra effort spent in developing these functions.

Reasoning Capability

In terms of reasoning consistency and efficiency, the prototype was not able to deal with complex cases satisfactorily, where the patient had multiple agents and/or therapeutic maneuvers. The problem was due to an excessive amount of processing and looping when numerous schemas were involved and/or created. The situation inadvertently caused memory-swapping to lock up, leaving program abortion as the only recourse. However, the control knowledge was clearly defined and separated from the other parts of the knowledge base. A comparison of the rules revealed only 44 out of 193, or 23%, were "protocol" rules. The remaining 77% were control-oriented, which included those that read input, compute and compare patient states, display output, and others that primarily maintain and update the knowledge base.

The separation of intervention strategies and choices appeared effective, since the line of reasoning was not obscured by the numerous physiologic patterns and therapeutic choices. By defining the intervention strategies and choices as schemas, one can easily expand their number without requiring additional rules. However, this was at the expense of having a restricted line of reasoning. For instance, the present system does not allow explicit sequencing of intervention strategies other than by time. There is no easy way to implement a strategy that would say "try treatment A first, if it does not work, then try treatment B ..." – which is an acceptable practice within the CVICU.

On the other hand, the use of computational drug-dosage response and net-difference scoring models tended to obscure the line of reasoning at times. Since the overall response was based on the current hemodynamic values and the expected effects of certain agents/dosages, any fluctuations in their values could impact the results. This was notable when the general drug-dosage response tables were updated with the actual effects from certain patients. Thus, depending on the current hemodynamic values and/or the averaged expected effects at the time, the prototype could propose to increase the dosage of an agent at one interval, only to then decrease it at the next.

Accuracy and Completeness

The overall accuracy and completeness of the test results appeared adequate. Although the performance acceptance level was only 62% when all five intervention groups were included, the averaged acceptance level for the fluid and bleeding intervention groups was 80%, being 89% for bleeding, offset by 71% for fluid. The prototype performed poorly in proposing electrolyte-replacement therapies, mainly caused by missing laboratory patterns – a problem easily rectifiable. The usage pattern for inotropes and vasoactive agents by the prototype and the staff was similar; both had acceptance levels averaging at 50%. Although unimpressive when compared with the fluid/bleeding intervention groups, the performance of the prototype was no worse than that of the staff.

The prototype addressed the issue of completeness satisfactorily. Specifically, it dealt gracefully with physiologic patterns outside of its knowledge, displaying them as unclassified patterns. For protocols not yet implemented, diagnostic tests such as check hypertension were used as place-holders to display the appropriate interventions needed.

CHAPTER 9

DISCUSSION

This chapter discusses the overall performance of the prototype, the knowledge representation and reasoning approach used, the prototype's technical design, the need for formalized therapeutic protocols in the clinical setting, the outstanding issues and a future work plan. The general intent of the discussion is to analyze the work undertaken and determine the value of the research within the context of intensive care medicine.

9.1 Overall Performance of the Prototype

The prototype validated 80% of the proposed therapies for fluid replacement and active bleeding (89% for bleeding; 71% for volume depletion). All of the figures were significantly superior to the therapies instituted by the staff: 44% overall (48% for bleeding; 40% for volume depletion). The significant differences could have led to some quality improvement if the automated protocols had been implemented when the patients were in the CVICU.

Closer examination of the protocol rules for bleeding shows these protocols were more straightforward. Specifically, the protocols were based on the detection of active bleeding through CT, coupled with abnormal laboratory levels in HB, HCT, PT, PTT and/or PLT. As long as such conditions prevailed, one should expect the protocols to be applied successfully. Where the protocols failed, they were attributed to easily rectifiable programming errors, e.g. erroneous interpretation of the cumulative CT levels. The main reason for the lower staff acceptance rate was the lack of formal guidelines to treat bleeding. An example is the over-eager use of protamine and/or fresh-frozen plasma for treating active bleeding with suspected coagulopathy. Sometimes this was done even when recent laboratory results indicated normal levels of PT and PTT.

Application of the protocols for fluid, vasoactive, inotropic therapies were more complicated; they required detection of hypovolemic hypotension, and selection of the agent based on drug-dosage response and net-difference computations. The current heuristics for deriving patient-specific dosage responses and net-difference scores were the main cause of unpredictability in the proposed interventions. In particular, the inconsistent dosage responses caused considerable variability in the net-score computation. Similarly, the min-max heuristic is a questionable method to combine the anticipated responses when multiple agents were being manipulated simultaneously. But there is little literature regarding the pharmacodynamics of cardiovascular agents and fluid therapies at the level of detail required by the algorithms.

The quantitative aspect of the drug-dosage response tables was also inherently problematic, having been constructed from the consensus of just two expert physicians. The addition of further experts and time would help, but accumulating quantitative data from a deployed system would likely be of much greater value. Technically, one may also devise multiple drug-dosage response and net-score computation algorithms that could be dynamically compared and reconciled based on some yet-to-be-defined criteria. An example of this type of multiple modeling is in forecasting, where results from several prediction models are averaged to reduce the magnitude of forecast errors (Buffa 1987).

Despite its poor performance, the use of patient-specific drug-dosage response and net-score computation is conceptually sound and was appealing to physicians. This is how a clinician would reason when planning and assessing therapy choices – by diagnosing the problem, proposing an appropriate treatment, assessing its effectiveness through observing the physiologic response, and amending the therapy where appropriate. The use of a composite index such as the net-difference score is not new: the best examples are those for deriving severity indexes in the ICU. However, the use of such indexing schemes for therapy management on a moment-to-moment basis has not been reported, and requires further investigation.

The 50% level of acceptance for the electrolyte replacement therapy was unexpected, but not inexplicable. Most errors were caused by missing laboratory patterns necessary for invoking the protocols. Other problems requiring further investigation included the prototype's inability to invoke the rules to redefine the target range, wean the use of therapeutic agents or propose the measurement of periodic cardiac output.

In general, the validation results of the prototype seem comparable to those of MYCIN during the early stages of its development and validation (Shortliffe 1985). In the evaluation of MYCIN, only 65% of its therapy recommendations were rated as acceptable by expert evaluators (the corresponding acceptance rating for the five specialists on the same cases was only 56%). From the perspective of progress, though, it was disappointing in that, despite the two decades that have spanned since the inception of MYCIN as one of the first medical expert systems, the development of expert decision support systems in clinical medicine still remains very much an art.

Attempts to compare the validation results with other similar systems were limited, as not many formal bench-testing results have been published. A retrospective study conducted at the LDS Hospital (East 1992) with 97 ICU patients to extract ventilatory management rules suggested the use of such cases for rule extraction was error-prone and not reliable. The finding was also supported by this study, where the expert CVICU physicians knew that some interventions had been based on manual PAWP measurements taken but not entered into the monitor network. Other decisions could have been based on bedside examinations not recorded in the chart, such as checking for edema and peripheral pulse. Nevertheless, informal comparison with other more advanced decision-support systems already in limited routine use are favorable. Examples include the expert ventilatory management system at the LDS Hospital (Henderson 1992) and ONCOCIN, an expert cancer therapy management system at Stanford University (Hickam 1985), which have both been evaluated to perform at an expert level with the acceptance of their therapy recommendations at 92 and 79%, respectively.

Factors affecting the performance of the expert ventilatory management system were timeliness and accuracy of the input data; in ONCOCIN they were due to the system's interpretation of the protocols, which tended to be rated as excessive by the expert physicians. In the prototype, the inappropriate therapeutic recommendations were due to the use of unverifiable heuristics and expert rules. Thus, our existing prototype requires substantial refinement and further testing before it can proceed with any field-trial in a clinical setting.

9.2 Knowledge Representation and Reasoning

A unique feature that distinguished the prototype from the expert ventilatory management system at the LDS Hospital is in the use of physiologic patterns. The patterns are the most important part of the prototype, since they serve to identify the clinical conditions present, and to invoke the corresponding therapeutic strategies and choices.

The successful use of pattern-recognition for diagnosis in the ICU has also been reported elsewhere. Examples include fault models where patterns of selective physiologic variables were classified to produce alarm signals (Beneken 1987); visual patterns of physiologic states in circular diagrams for diagnosis of shocks (Siegel 1983); severity index score for identification of abnormal physiologic functions (Bland 1983); the sequential clinical scenes for hemodynamic monitoring (Cohn 1986). Perhaps the most comprehensive pattern-recognition system developed to date is that of the QMR consultation system for internal medicine, where the clinical findings for over 600 diseases are stored as binary bit-map patterns for rapid retrieval purposes (Miller R 1986). However, little has been reported on the use of patterns for automated therapeutic management.

In the prototype, 466 patterns were classified from the learning cases. Another 101 unknown patterns were identified during the validation of the test cases, i.e. an addition of 22%. One would expect the number of unknown patterns to decrease rapidly as new cases are added. While the 5-digit pattern code allows over 32,000 permutations, analysis of the 26 historical cases only revealed 567 patterns in total – a rather small fraction quite manageable for routine use.

Distinctive in our prototype is the separation of the intervention strategies from choices, which allows easier control of the reasoning process. Thus, the protocol rules only need to be defined once and not repeated with the individual patterns. The maintenance of the patterns becomes easier since they can be added by creating the corresponding schema without being concerned with the reasoning process. This approach is similar to that used in VQ-ATTENDING (Miller 1985), which explicitly separated strategic knowledge about treatment goals from tactical knowledge about management choices for achieving those goals. The advantage as reported by Miller, is to allow a more comprehensive and logical set of goals to be defined independent of the logistics and management.

The use of computational models in the prototype is an illustration of using multiple knowledge sources for clinical problem-solving. Examples were the exponential smoothing average and the drug-dosage response models, where the quantitative nature of the physiologic data and their pharmacodynamic relationships with therapeutic agents were exploited to the fullest. The inclusion of computational models extends beyond the use of experiential knowledge, which is mostly qualitative and subjective. This is where the computer can supplement the qualitative problem-solving skills of clinicians by providing quantitative manipulation of multiple physiologic variables, a task which is difficult and impractical to do manually at the bedside.

Many expert systems that include the use of quantitative knowledge have been described. Examples include the IFRID hybrid rule-based expert system that is capable of continual experiential update through a statistical database (Hughes 1990); the KUSIVAR knowledge-base support system for mechanical ventilation that uses a mathematical model for optimal arterial oxygenation (Rudowski 1989); the ONYX cancer therapy planning system is an ONCOCIN extension that combines decision theory, simulation and AI planning techniques to derive complex therapy plans (Langlotz 1986). Such quantitative approaches were reported to have greatly expanded the capability of expert systems to include domains and problems that are inherently quantitative, uncertain with a continuum of solutions; these are also situations that cannot be easily addressed by expert rules alone.

The use of different states to represent the patient's conditions over time was explored in the prototype, as was specific schemas to keep track of instituted and proposed interventions being processed. These approaches are not new; VM was the first expert system for ICU ventilation management that used state transition to model the patient's condition over time (Fagan 1985). COMPAS (the earlier version of the ventilation management system at the LDS Hospital) used a blackboard architecture that had similar knowledge structures (Sittig 1989a & b). Another was the representation and handling of temporal information in ONCOCIN (Kahn 1985). A problem with these knowledge structures is that their maintenance is inherently complex, as was the case with the prototype. However, judging from the inconsistent recommendations made in some of the test cases, it may be necessary to include compiled causal rules based on known physiologic models. Despite the added complexity, the use of causal knowledge should improve the consistency of the patient states and the therapy recommendations over time.

Perhaps the most complicated aspect of the prototype is its reasoning process, which is entirely deterministic. The reasoning process consists of rules and schemas that tightly control the rule firing sequence. Though an effort was made to separate the control knowledge from the domain knowledge, there was a tradeoff between the ease of manipulating the domain knowledge and the flexibility of the reasoning process. Presently, any change to the reasoning process would precipitate modification of the control rules, which proved to be a major undertaking during the initial development of the prototype.

Nevertheless, the conceptual decision framework of the prototype is sound and can be easily expanded to include other clinical problems in the CVICU, e.g., cardiac dysfunction, pulmonary hypertension, sepsis and renal failure. The process of classifying the patterns, matching the clinical conditions and developing the therapeutic protocols would be identical to the one with hypovolemic hypotension. The use of the historical CVICU cases were invaluable in the construction and validation of the prototype, and will likely continue to be the method to incorporate other clinical problems into the knowledge base.

9.3 Technical Design Considerations

Regarding the technical design of the knowledge representation scheme, the resulting knowledge structure adequately represented all relevant aspects of hypovolemic hypotension and therapeutic management at the proper granular level. Evidence includes the relative ease of expert physicians in understanding the reasoning process, and the ability of the prototype to provide recommendations using only the information and knowledge given. Nonetheless, the knowledge base is considered a surface model, without underlying cardiovascular or general physiologic knowledge. The use of causal knowledge based on physiologic modeling would have increased the complexity of the prototype and did not seem warranted. However, this premise could change over time, especially if clinial cardiovascular models representing the patient's states over time can be constructed. Once developed, it would be feasible to use expert rules and computational modeling from the surface model for solving routine problems, but to resort to the causal model in situations where the underlying physiology of the clinical problem is needed (Patil 1988).

The technical design of the reasoning process was ad-hoc in nature, adapting as much as possible to the decision-making steps that were deemed logical to the human experts. As such, the overall control structure is not entirely robust, and it is not certain whether this reasoning approach is adequate for managing other types of clinical problems within the intensive care domain. Unfortunately, AI and expert systems research has provided few consensus or standards. An early analysis of MYCIN (Clancey 1983) offered the clear separation of the three types of knowledge – the domain, control and support knowledge. The last knowledge type referred mainly to the nomenclatures necessary to express the first two within the system. The Arden syntax (Clayton 1989) provided some guidelines on knowledge structure and reasoning when developing expert systems, but at present the syntax applies to individual rules only, with no resolution on the design of more complex systems, especially those involving the use of protocols. The episodic skeletal-plan refinement approach used in ONCOCIN (Tu 1989) allowed the selection of therapeutic protocols, but it appeared too language-, platform- and domain-specific to be adapted to other areas, such as the CVICU. Currently, the design of any reasoning and control process in protocol-based expert decision-support systems remains the responsibility of the knowledge engineer.

The use of the commercial ARTIM expert system shell strongly influenced the technical implementation of the prototype. The absence of any database-access capability within ARTIM forced the use of schemas as the only form of patient database, with only a minor use of the external sequential text-file feature. It is questionable whether the object-oriented approach to developing expert decision-support systems can scale up in a production environment, if one has to deal with numerous patient and other records. The design choice is especially important if one were to integrate the decision-support system with the traditional hospital information system (HIS), which is mostly database oriented (Kwa 1987).

The size of the knowledge base developed in this study is trivial when compared to other well-established systems such as QMR, the expert consultation system for internal medicine, which contains over 40,000 pieces of relations and entities. Nevertheless, the prototype was not able to complete analyzing the more complicated test cases and had to be aborted after running for 24 hours. This is a cause for concern, since the prototype was already running on a SUN workstation with 24 MB main memory and 60 MB of swap space, with over 400 MB disk storage capacity. The lack of indexing and database-access capabilities in ARTIM was the crippling factor, since much of the reasoning process resorted to repetitive looping through the hundreds of schemas defined within the knowledge base. The size of the knowledge base would have been much smaller had ARTIM been able to access external databases, where most of the patterns, conditions and drug schemas could have been stored. Also, the processing time would have shortened if ARTIM had provided indexing of its schemas, allowing schemas to be referenced directly, rather than through its existing "For ... do ..." looping construct.

Considering the knowledge for treating hypovolemic hypotension constitutes less than a tenth of the entire CVICU domain, it would seem impossible to further expand the prototype under the existing implementation without rendering it totally inoperable for some cases. The proposed solution is to adopt an integrated database approach where most of the knowledge bases are stored in the database, which in turn can be accessible by the expert system module during the reasoning process.

9.4 Use of Formalized Therapeutic Protocols

In recent years, there has been an increasing focus on protocolized care. This idea is not new, but is an umbrella label for practice algorithms, protocols, guidelines, standards and other terms about appropriate clinical care (IOM 1992). Perhaps the most familiar form of protocolized care is the use of logic flowcharts and algorithms for depicting the provision of care under different clinical situations. Examples include the decision-tree algorithms for fluid management in the ICU (Shoemaker 1985) and for the management of hypotension in the CVICU patient (Modry 1986). In these algorithms, conditional branches based on the results and patterns of certain physiologic measurements are provided to show the diagnoses and interventions required under a given set of clinical conditions.

A more elaborate form is the use of formal protocols, where guidelines for interventions are pre-defined relative to a specific circumstance, which may be further customized for the individual patient. An example is the manual post-operative doctor's order and nursing care protocol sheets used in the CVICU at the UAH, which allow the provision of patient-specific therapeutic agents, target physiologic parameter settings, and types of nursing care required. Another recent approach is the use of care maps, which explicitly state the expected outcome for each type of clinical problem, after provision of certain therapeutic interventions. For instance, in the manual ICU care map for treating uncomplicated myocardial infarcts, the goal for treating ischemia is to have the patient pain-free by the second day of hospitalization (Griffith 1992).

Probably one of the most ambitious efforts to date in formalizing care is by the Institute of Medicine (IOM) in United States, which has developed a general framework for the provision and evaluation of clinical practice guidelines (IOM 1992). The framework includes the rationale for practice guidelines, the definitions on the different types of guidelines and their attributes, the methods and procedures to developing the guidelines, and an assessment instrument to certify the soundness of particular guidelines. The need for practice guidelines is obvious according to IOM: wide variations exist in practice patterns and use of health services, while research indicates inappropriate use of many interventions and services, for which the outcome are uncertain in many cases.

The IOM position is particularly relevant to this research study. For instance, during the development of therapeutic protocols, the use of crystalloid versus colloid remained a controversial issue, even after the consensus to use crystalloids unless a colloid was clearly justified (e.g. albumin, for edema and chronic obstructive pulmonary disease). Another was the preferred level of base deficit requiring treatment, which varied from -2 to -4 units depending on the physician. Similarly, the current practice of administering topical nitropaste Q4H as a standing order after the patient is weaned from nitroglycerine has been a tradition rather than rational judgment.

Even where manual protocols were in place, many physicians pursued other paths unscrutinized prior to the review from this study. Examples included the simultaneous weaning of patients from multiple agents, the lack of or inaccurate hemodynamic target range definition, and the inadequate frequency of cardiac output assessment. These conditions represent quality improvement opportunities that could be exploited if some detailed practice guidelines or protocols were established. More importantly, the use of formal protocols is a necessary pre-requisite to being able to systematically compare the relative effectiveness of interventions and their impact on patient outcome in the CVICU.

A computer is not a necessity for formalized protocols and care plans (and must not be unyieldingly rigid when it is). However, flowcharts and other formalized documents for manual use must be modest in complexity to be practical. Even the physical document size must be restricted. With care maps, the range of exceptions challenges human usage. And it must be remembered that all such documents have to be used routinely at the bedside in a clinical setting.

Automated protocols, on the other hand, hold some promise in their ability to improve the quality of care. A 2-year randomized clinical trial conducted at Regenstrief Institute found a 400% increase in the delivery of preventive care associated with the use of the reminder system (McDonald 1984). Researchers at the LDS Hospital in Utah have reported significant improvements in the quality of care with the use of computer-based therapeutic protocols (Pestotnik 1990, Elliott 1991). But it is important to note that the most successful systems to date are all integrated with the HIS. The types of decision-support offered by these systems are mostly reminders and alerts for exception conditions, embedded controls for therapeutic interventions, decision-assistance for order processing, and identification of high risk patients, based on information already within the HIS.

9.5 Outstanding Issues

Several outstanding issues remain: validity and reliability of the computational models for calculating dosage response and net-difference scoring; need for group consensus among CVICU physicians on the protocols; prototype refinement and enhancement of additional features; call for a major technical design review on the prototype's architecture; influence on the users of their perceived value of decision-support systems. These issues are discussed below.

As noted earlier, the validity and reliability of the drug-dosage response model came into question during the testing of the prototype. In particular, the min-max algorithm needs to be revised and possibly replaced by other more sophisticated means of combining the effects of changing multiple agents. The net-difference scoring algorithm used to select a therapeutic agent needs additional heuristics to improve its ability to handle unique situations. An example is to prefer the existing therapy instead of an alternate with a lower net-score, if the current hemodynamics are believed to be inaccurate. The adaptive model for the drug-dosage response tables was also problematic as it affected the consistency of the therapeutic recommendations. The dynamic behavior of the drug-dosage response model should be further investigated.

Only individual consensus on the protocols was obtained from the four expert CVICU physicians. This was done by meeting with the physicians and reviewing the written protocols with them, explaining the rationale of the protocols, and seeking their concurrence during the process. The physicians accepted the protocols in principles, but expressed concerns in some of the protocol rules, such as the use of colloid versus crystalloid and of bicarbonate. No group meetings have been held to discuss these concerns and finalize the protocols; this would be a necessary step before any clinical trial.

Sensitivity analysis should be conducted on the prototype to determine its behavior under varying parameter settings. For instance, the severity weight factors used in determining the net-difference score could be altered to observe any change in the system's performance. The patient-specific drug-dosage response update algorithm could be de-activated to compare the results when only the general dose response tables were used. The validation guidelines could also be modified to determine if they would make any difference in tallying the responses.

Other features not considered in the initial prototype may be contemplated as part of the refinement process. The features include automatic setting of initial target ranges when given the pre-, intra- and post-operative data, use of different assessment schedules for evaluating therapeutic agents based on maximal effect durations, and adoption of the Arden syntax (Clayton 1989) to standardize the expert rules. The nursing notes on re-zeroing, repositioning, and the time of chest X-rays, etc. collected during the chart review could be incorporated into the system as simulated user input in response to action proposals by the prototype. These enhancements are all intended to provide more flexibility and increased functional capability for the prototype.

An important issue is the technical implementation of the prototype in ARTIM, which in its present form is inappropriate for further expansion. The most serious problem lies in the prototype's inability to handle complex cases without locking up the system, which would be totally unacceptable in a clinical environment. A related issue is the need to eventually integrate this decision-support system with the HIS to access other patient data in a real-time fashion, such as demographics and care plans. A major move towards using a database approach is suggested, where much of the static knowledge base and dynamic patient schemas can be stored as database records. The continued reliance on ARTIM is questionable, since it does not provide any external database access routines (nor is it equipped with any tools for building a window-based user-interface). However, until a decision can be made, the immediate goal should be to continue with the prototype under the existing system environment to improve its performance level.

Perhaps the most important issue is the perceived value of this type of decision-support system in a clinical setting. Although results from the retrospective validation process demonstrated the prototype can better manage hypovolemic hypotension, the ultimate success of such a system is dependent on factors beyond that of validity testing. Three issues come to mind, the first being the credibility of the system, which relies on the accuracy, reliability, consistency and acceptability of the protocols. Establishing this credibility requires the ongoing participation of influential clinical staff to develop and maintain the protocols. Second, for the system to be accepted into routine use, one must demonstrate the system can lead to an improvement in the quality of care and possibly patient outcome. Thus, ongoing evaluation of the system must be planned and executed. Once the benefits of this system can be demonstrated, its acceptance by the staff would be almost assured. Although the study did not address the need for an effective user interface, this would be the third issue requiring attention, before the prototype is implemented as a bedside system for routine use.

9.6 Future Work Plan

The future work plan outlined in this section is a summary of the outstanding problems and issues identified. The plan is organized as a task list to allow future system developers to continue with the study in preparation for eventual field trial. An assumption was that, for the immediate future, the study would continue under the existing environment. The tasks are summarized as follows:

Refine the Prototype.

The validation of the test cases led to the identification of problem areas requiring further investigation and refinement. Examples include the computational models for dosage response and update calculations, net-difference scoring, and any programming logic errors encountered during the testing of the cases.

Conduct Sensitivity Analysis.

Sensitivity analysis should be conducted to determine the impact of changing selected configuration settings on the performance of the prototype. Examples include the use of different severity weight factors for net-score computation and modified validation guidelines.

Review the Results with the Experts.

The expert CVICU physicians should review the test cases again with the output from the prototype. The review would allow the appropriateness of the proposed interventions to be more accurately determined.

Run the Test Cases as a Learning Set.

The test cases should now be used as a second set of learning cases where the unknown patterns are matched to conditions and interventions, and incorporated into the knowledge base.

Seek Group Consensus on the Protocols.

The expert CVICU physicians should meet as a group to discuss any concern with the protocols and finalize them. Efforts should be underway to begin developing protocols for other clinical problems within the CVICU, such as cardiac dysfunction, pulmonary hypertension, sepsis and renal failure. It is important to keep up the momentum as enthusiasm could wane after a prolonged period of inactivity.

Enhance the Prototype.

Features not implemented in the initial prototype should now be reviewed and incorporated as a second version to enhance the prototype's functionality. Examples include automatic initial target range definition, variable assessment schedules for therapeutic agents, adoption of the Arden syntax and simulated user input from selected nursing notes.

Prepare Additional Test Cases.

Additional historical CVICU cases should be collected for a second-stage bench-testing, using the same approach as before. This stage is highly recommended since the first validation exercise did not prove entirely satisfactory, in that the prototype's performance was impeded by errors that should be resolved. Proceeding directly to field-testing is not advised at this stage.

Review the Technical Design.

An important decision has to be made in terms of whether or not to continue development of the prototype under the current platform, i.e. using ARTIM as the knowledge programming tool and the Unix-based SUN workstation as the computer system. The decision would impact the technical implementation of the next version of the prototype.

CHAPTER 10

SUMMARY AND CONCLUSIONS

The efforts to develop and validate a decision-support system prototype for hemodynamic management of hypovolemic hypotension in CVICU patients have been described in the preceding chapters. A summary description is provided in this chapter of the work done and the conclusions drawn as a result of the study.

The hypothesis in the study was that expertise in hemodynamic management can be formalized as computer-based protocols, which can provide therapeutic recommendations significantly more consistent with clinical management goals than occurs with current practice. The hypothesis was tested retrospectively on historical CVICU cases, where therapeutic interventions for hypovolemic hypotension proposed by the prototype and those instituted by the staff were compared in parallel against expert critiques on the same cases for significant differences.

The goals of the research study were to formalize the hemodynamic management expertise, construct a functional computer prototype containing the encoded expertise, conduct formal bench-testing to validate the prototype's performance with interventional events from historical CVICU cases, and discuss the problems and issues in using computer-based protocols.

The formalization process consisted of constructing a conceptual framework for managing hypovolemic hypotension, collecting hemodynamic and clinical data from historical 40 CVICU cases for learning and testing, constructing a set of therapeutic protocols and critiquing 410 interventions from 13 of the cases with two expert CVICU physicians, seeking consensus on the protocols with two other expert physicians, and encoding the formalized expertise in a computer prototype.

Validation of the prototype was done with 399 interventions from another 13 historical CVICU cases. The results showed that the proposed therapies for fluid replacement and bleeding from the prototype were significantly better than those instituted by the staff relative to the expert critiques (80% versus 44%, respectively). Based on the validation results, the null-hypothesis that the proportions of consistent interventions were equal among the prototype and the staff was rejected. Further analysis suggested that the prototype provided recommendations and critiques that might have improved the quality of care if it had been available when the patient was still in the CVICU. The introduction of this type of decision-support systems into the clinical setting also appeared timely, as there has been an increasing effort to establish standards in the delivery and assessment of care to improve its quality and outcome.

In conclusion, it is believed the work presented in this dissertation has made a contribution to the field of medical informatics. Specifically, the study has demonstrated the use of multiple knowledge sources, ranging from physiologic pattern-matching, therapeutic protocols, expert reasoning heuristics, to computational drug-dosage response modeling, in a computer prototype to provide alerts, critiques and therapeutic recommendations. The resulting prototype performed significantly better than the current practices within the CVICU in managing fluid replacement and active bleeding in hypovolemic hypotension. The conceptual framework and the reasoning process of the prototype are both sound and capable of being expanded to include other clinical problems in the CVICU. The study has also reaffirmed the need to seek consensus and buy-in from the clinical staff, especially the physicians, in terms of developing and maintaining the protocols on an ongoing basis.

Most importantly, the perceived value of this type of decision-support system by its ultimate users cannot be over-emphasized. One must continually seek to demonstrate that the system can improve the quality of care and possibly patient outcome within the routine clinical setting through rigorous scientific experimentation and formal evaluation.

GLOSSARY

ABG	arterial blood gases
ABPD	arterial blood pressure diastolic
ABPM	arterial blood pressure mean
ABPS	arterial blood pressure systolic
AI	artificial intelligence
AI/Rheum	AI/Rheumatology expert system by Kingsland L, Bethesda
ARDS	adult respiratory distress syndrome
ARTIM	automated reasoning tool - information management
BSA	body surface area
CABG	coronary artery bypass graft
Ca	calcium
Cl	chloride ions
CO	cardiac output
CT	chest tube drainage or loss
CV	cardiovascular
CVD	cardiovascular disease
CVICU	cardiovascular intensive care unit
CVP	central venous pressure
CVP/ART line	central venous pressure/arterial line
DSS	decision-support system
DTA	digitalis therapy advisor
D5W	dextrose 5% water
DXplain	diagnostic prompting system by Cimino J.
EDP	end-diastolic pressure
EDV	end-diastolic volume
filling pressures	include central venous pressure and pulmonary diastolic pressure
H	hydrogen ion
HB	hemoglobin
HCO3	bicarbonate ions
HCT	hematocrit
HP	Hewlett Packard
HR	heart rate
ICU	intensive care unit
I/O	intake/output (refers to fluid)
intra-op	intra-operative stage, being post induction
ion-Ca	ionized calcium
K	potassium ions
FFP	fresh-frozen plasma
LAP	left atrial pressure
LHS	left hand side
LOS	length of stay
LV	left ventricular
LVEDP	left ventricular end-diastolic pressure
MAP	mean arterial pressure
Mg	magnesium ions
MYCIN	medical expert system by Shortliffe, Stanford University
Na	sodium ions
NCSS	numerical cruncher statistical system
ONCOCIN	a cancer therapy management system from Stanford University

OSM	osmolality
PAD	pulmonary arterial diastolic (pressure)
PAPD	pulmonary arterial pressure diastolic
PAPM	pulmonary arterial pressure mean
PAPS	pulmonary arterial pressure systolic
PAWP	pulmonary arterial wedge pressure
PDMS	patient data management system
PLT	platelets
PTT	partial thromboplastin time
PT-INR	prothrombin time - ratio
PVRI	pulmonary vascular resistance index
pCO2	partial carbon dioxide pressure
pO2	partial oxygen pressure
post-op	post-operative stage
pre-op	pre-operative stage
QMR	quick medical reference by Miller R from University of Pittsburgh
RHS	right hand side
SI	stroke index
SV	stroke volume
SVRI	systemic vascular resistance index
UAH	University of Alberta Hospitals in Edmonton, Alberta
VAMA	ventricular arrhythmia management advisor by Gorry
VO2	oxygen consumption
VQ-ATTEND	critiquing system for ventilatory management by Miller PL, Yale University
WT	weight

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APPENDICES

APPENDIX A – CVICU FLOWSHEET

APPENDIX B – THERAPY GUIDELINES USED IN THE CVICU AT UAH

APPENDIX C – CRITERIA FOR DATA COLLECTION

APPENDIX D – PROPOSED THERAPEUTIC PROTOCOLS FOR CVICU

APPENDIX E – EMPIRICAL DRUG-DOSAGE RESPONSE TABLES

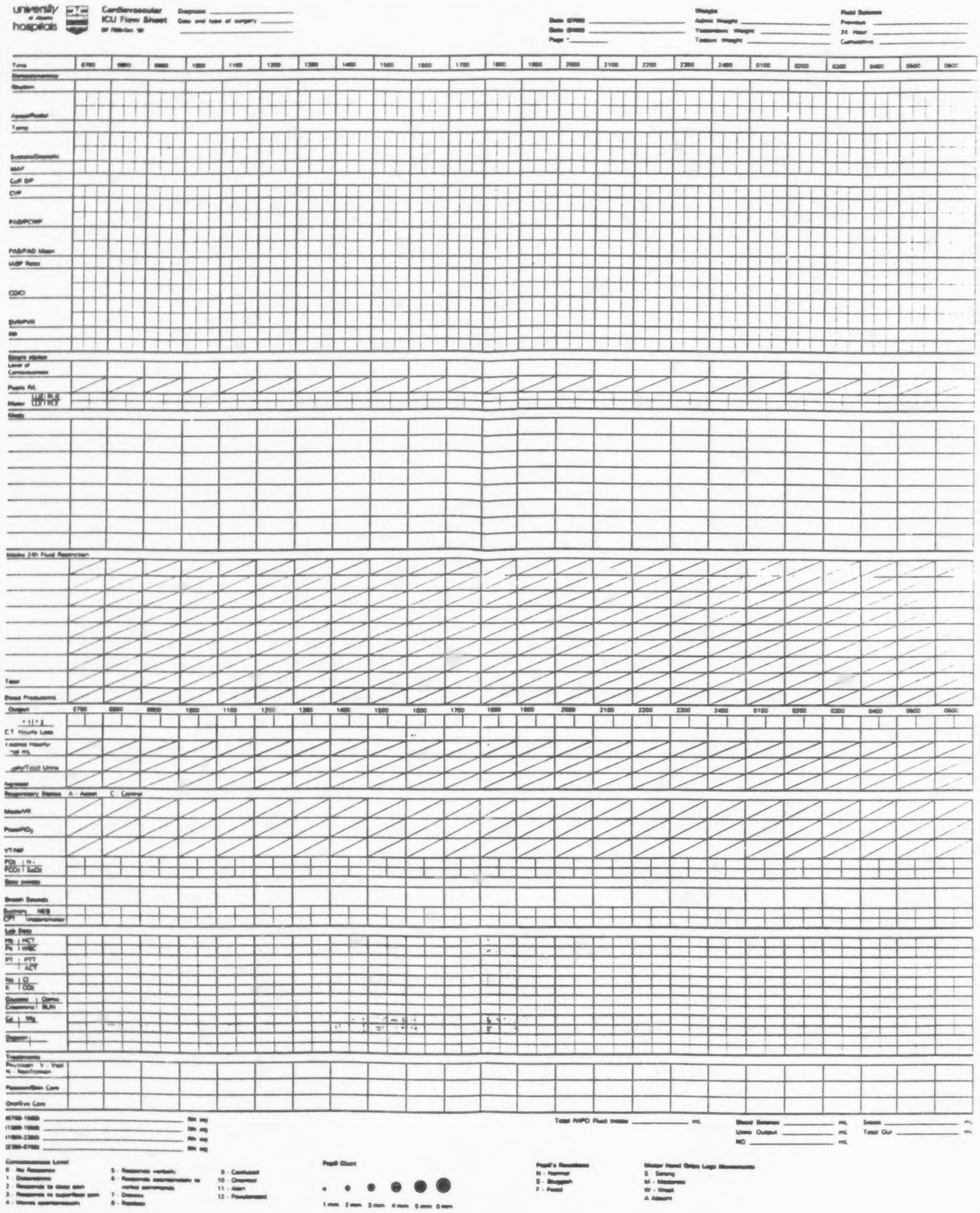
APPENDIX F – COMPUTATIONAL DRUG-DOSAGE RESPONSE TABLES

APPENDIX G – REVERSE PROTOCOLS

APPENDIX H – TECHNICAL DESCRIPTION OF THE PROTOTYPE

APPENDIX A – CVICU FLOWSHEET

The CVICU flowsheet used at the University of Alberta Hospitals



APPENDIX B – MANUAL PROTOCOLS USED IN THE CVICU AT UAH

manual protocol sheets not included

Pages 176-181 inclusive have been removed due to poor print quality.

APPENDIX C – CRITERIA FOR DATA COLLECTION

NAME OF DATA VARIABLE	SOURCE	TYPE	INTERVAL
Diastolic/systolic/mean ABP	hemodynamic	post-op	minute
Cardiac index/cardiac output	hemodynamic	post-op	4-6 hours or as needed
Central venous pressure	hemodynamic	post-op	min, 1/4-6 hrs or as needed
Heart rate	hemodynamic	post-op	minute
Left/right cardiac work indexes	hemodynamic	post-op	4-6 hours or as needed
Left/right vent.stroke indexes	hemodynamic	post-op	4-6 hours or as needed
Pulmon systolic/diastolic/mean	hemodynamic	post-op	min, 1/4-6 hrs or as needed
Stroke work/stroke index	hemodynamic	post-op	4-6 hours or as needed
Pulmonary vascular resist.index	hemodynamic	post-op	4-6 hours or as needed
Systemic vascular resist.index	hemodynamic	post-op	4-6 hours or as needed
Pulse rate	hemodynamic	post-op	minute if attached
Hemoglobin / Hematrocrit	laboratory	pre-op/post-op	daily or as needed
White blood cells, platelets	laboratory	pre-op/post-op	daily or as needed
Serum potassium	laboratory	pre-op/post-op	2 hours or as needed
Serum magnesium	laboratory	pre-op/post-op	daily or as needed
Prothrombin/partial time	laboratory	pre-op/post-op	daily or as needed
Serum Na,Cl,CO2,Osmol	laboratory	pre-op/post-op	6 hours or as needed
Serum creatinine, BUN	laboratory	pre-op/post-op	6 hours or as needed
Albumin,total protein	laboratory	pre-op/post-op	1-2 day or as needed
Ionized calcium, calcium	laboratory	pre-op/post-op	4-6 hours or as needed
Creatine kinase, phosphate	laboratory	pre-op/post-op	1-2 day or as needed
Resp mode, ventilation rate	ventilation	post-op	when adjusted
Fraction of inspired oxygen	ventilation	post-op	when adjusted
Pos. peak expiratory pressure	ventilation	post-op	when adjusted
peak inspiratory pressure	ventilation	post-op	when adjusted
Arterial oxygen saturation	blood gases	pre,intra,post	2-4 hours or as needed
partial oxygen tension	blood gases	pre,intra,post	2-4 hours or as needed
partial carbon dioxide tension	blood gases	pre,intra,post	2-4 hours or as needed
Hydrogen ions	blood gases	pre,intra,post	2-4 hours or as needed
Base excess	blood gases	pre,intra,post	2-4 hours or as needed
Bicarbonate	blood gases	pre,intra	as needed
Temperature	blood gases	pre,intra,post	2-4 hours or as needed
Ejection fraction	cath lab	pre-op	once
Cardiac index, end-systolic vol.	cath lab	pre-op	once
Left-vent end-disatolic vol/pres	cath lab	pre-op	once
Systolic,diastolic,mean ABP	cath lab	pre-op	once
Wedge pressure	cath lab	pre-op	once
Heart rate	cath lab	pre-op	once
Body surface area	patient	post-op	4-6 hours
Surgical procedure	patient	pre-op	once
Length-of-stay	patient	post-op	once
Height	patient	pre-op,post-op	once
Weight	patient	pre,intra,post	daily or as needed
Urine, chest-tube & others	Output	post-op	hour,cumulative 24 hours
Blood products	Input	post-op	as needed
IV fluids	Input	post-op	as needed
Therapeutic interventions	Input	post-op	as needed

Data variable choices from the CVICU cases in this study. Cath lab is catheterization laboratory.

CARDIOVASCULAR INTENSIVE CARE: MEDICAL CHART DATA COLLECTION
DATA COLLECTION INSTRUCTIONS AND GUIDELINES

I. DATA COLLECTION ENVIRONMENT

A. LOCATION
  1. University of Alberta Hospitals Medical Records Department
  2. Research cubicle within Medical Records assigned for data collection

B. CHART AUDIT TIME FRAME
  1. April 1, 1992 to September 18, 1992

II. SAMPLE

A. 60 medical charts consisting of all CVICU inpatient admissions during the summer of 1991

B. INCLUSION CRITERIA
  1. patients whose surgical procedure is "Coronary Artery Bypass Graft"

B. EXCLUSION CRITERIA
  1. patients whose length-of-stay exceeds four days
  2. patients with Intra-aortic Balloon Pumps

III. COMPUTER INFORMATION

A. Data is to be collected using
  1. a NBCC notebook computer
  2. Lotus 123W Software

IV. SETUP - PRE-CVICU DATA [Filename: AUDIT.WK3]

A. Cardiac Catheterization Record
  1. Record the following data as entered on the cardiologist's consulting letter and/or cardiac catheterization report:
    a. Ejection Fraction
    b. ESV
    c. Cardiac Index
    d. LVS (at rest)
    e. LVE (at rest)
    f. AOS (at rest)
    g. AOD (at rest)
    h. AOM (at rest)
    i. BSA
  2. Record all medications, according to the pre-set code list, that were prescribed at the time of the cardiac catheterization

B. Pre-operative Vital Signs
  1. Record the following data as entered on the admitting nursing history:
    a. height (cm)
    b. weight (kg)
    c. systolic/diastolic blood pressure (mmHg)
    d. heart rate (bpm)
    e. respiratory rate (rpm)
    f. temperature (øC)

C. Pre-operative Laboratory Results
  1. Using the cumulative laboratory result sheets, record the following results obtained at the time of the patient's admission to hospital:
    a. WBC
    b. HGB
    c. HCT
    d. PLATELET CT
    e. PT
    f. PTT
    g. NA
    h. K
    i. CO2
    j. OSMO
    k. BUN
    l. CREATININE
    m. GLUCOSE
    n. IONIZED CA
    o. CA
    p. PHOSPHATE
    q. MG
    r. CK
    s. TOTAL PROTEIN
    t. ALBUMIN

  2. If the patient was admitted for a period longer than a week prior to surgery, then also record any laboratory results obtained in the three days prior to surgery

Pre-operative Laboratory Results Notes:
  1. Transcribe numerical results to the same number decimal places as shown

    on the cumulative laboratory sheets
2. Enter the date and time of the laboratory result as given on the cumulative sheets
3. Note in the TEXT column "Specimen hemolyzed" if so indicate on sheets

D. Pre-operative Blood Gas Results
1. Record the following data according to the blood gas requisition forms:
    a. Date and time of blood gas analysis.
    b. Ventilator Mode (if applicable)
    c. SIMV rate (if applicable)
    d. PEEP (if applicable)
    e. FiO2 (if applicable)
    f. O2 SAT
    g. PO2
    h. PCO2
    i. H+
    j. PH
    k. SaO2
    l. Base Excess
    m. HCO3
    n. Temperature

2. If the patient was admitted for a period longer than a week prior to surgery, then also record any blood gas results obtained in the three days prior to surgery

E. Intra-operative Vital Signs
1. Record the following data as entered on the anesthetic record upon arrival in the OR and immediately following the pump run:
    a. Temperature
    b. Systolic/diastolic blood pressure
    c. Heart rate
    d. MAP
    e. CVP
    f. PCWP

F. Intra-operative Laboratory Results
1. Using the cumulative laboratory result sheets, record the following data for the entire intra-operative period:
    a. WBC
    b. HGB
    c. HCT
    d. PLATELET CT
    e. PT
    f. PTT
    g. NA
    h. K
    i. CO2
    j. OSMO
    l. CREATININE
    m. GLUCOSE
    n. IONIZED CA
    o. CA
    p. PHOSPHATE
    q. MG
    r. CK
    s. TOTAL PROTEIN
    t. ALBUMIN
    u. BUN

Intra-operative Laboratory Results Notes:
1. Transcribe numerical results to the same number of decimal places as shown on the cumulative laboratory sheets
2. Enter the date and time of the laboratory results as given on the cumulative sheets
3. Note in the TEXT column "Specimen hemolyzed" if so indicate on sheets

G. Intra-operative Blood Gas Results
1. Record the following data according to the blood gas requisition forms:
    a. Date and time of blood gas analysis.
    b. Ventilator Mode
    c. SIMV rate
    d. PEEP
    e. FiO2
    f. O2 SAT
    g. PO2
    h. PCO2
    i. H+
    j. PH
    k. SaO2
    l. Base Excess
    m. HCO3
    n. Temperature (øC)

2. Record the results obtained upon the patient's arrival in the OR and immediately following the pump run

H. Post-operative Vital Signs

- 1. Record the following data as entered on the anesthetic record prior to the patient leaving the OR:
  - a. Temperature
  - b. Systolic/diastolic blood pressure
  - c. Heart rate
  - d. MAP
  - e. CVP
  - f. PCWP

I. Post-operative Laboratory Results

- 1. Using the cumulative laboratory result sheets, record the following data for the entire length-of-stay in CVICU:
  - a. WBC
  - b. HGB
  - c. HCT
  - d. PLATELET CT
  - e. PT
  - f. PTT
  - g. NA
  - h. K
  - i. CO2
  - j. OSMO
  - l. CREATININE
  - m. GLUCOSE
  - n. IONIZED CA
  - o. CA
  - p. PHOSPHATE
  - q. MG
  - r. CK
  - s. TOTAL PROTEIN
  - t. ALBUMIN
  - u. BUN

J. Post-operative Blood Gas Results

- 1. Transcribe the following data according to the white blood gas forms as recorded on the anesthetic record prior to the patient leaving the OR:
  - a. Date and time of blood gas analysis.
  - b. Ventilator Mode
  - c. SIMV rate
  - d. PEEP
  - e. FiO2
  - f. O2 SAT
  - g. PO2
  - h. PCO2
  - i. H+
  - j. PH
  - k. SaO2
  - l. Base Excess
  - m. HCO3
  - n. Temperature (øC)

V. SETUP - POST-OPERATIVE DATA [Filename: AUDIT.WKZ]

A. Post-operative Physician Orders

Record the following data:

- 1. Section: I. Nursing Care, Item 5
  - a. CVP range in mmHg
  - b. PAD range in mmHg
  - c. PAWP range in mmHg
  - d. LAP range in mmHg
  - e. Replacement for Hct levels less than 28
- 2. Section: II. VENTILATORY MANAGEMENT, Items 1 and 3
  - a. Ventilator settings: % FiO2, Effective VT, SIMV frequency, PEEP, and maximum PIP
  - b. Weaning protocol: maximum FVC, minimum PO2, and maximum PCO2
- 3. Section III. I.V.THERAPY, Items 5,6,7,8, and 9
  - a. Dopamine concentration, minimum MAP, start, minimum, and maximum rates
  - b. Dobutamine conc, minimum MAP, start, minimum, and maximum rates
  - c. Epinephrine conc, minimum MAP, start, minimum, and maximum rates
  - d. Sodium Nitroprusside conc, max MAP, start, min, and max rates
  - e. Nitroglycerin conc, max MAP, PADP, and start, min, and max rates
- 4. Section: IV. PARAMETERS - NOTIFY CV RESIDENT FOR Items 3,4,5,6,7, 17
  - a. MAP range in mmHg
  - b. CVP range in mmHg
  - c. PADP range in mmHg
  - d. PAWP range in mmHg
  - e. LAP range in mmHg
  - f. maximum Serum Creatinine level

B. Transfer Physician Orders

- 1. Section: I. NURSING CARE, Item 1b
  - a. Ventilator settings: % FiO2, Effective VT, SIMV frequency, PEEP,

        maximum PIP
    b. Weaning protocol: maximum FVC, minimum PO2, and maximum PCO2
    c. Resident call protocol: maximum PCO2 and end tidal CO2
2. Section: IV. PARAMETERS - NOTIFY CV RESIDENT FOR, Items 2,3
    a. Heart rate range
    b. Systolic pressure range

SETUP - POST-OPERATIVE DATA NOTES:

1. Transcribe numbers as written. Omit any indecipherable data with an explanatory note.
2. Record the date and time if they are hand-written on the Doctors Orders sheets. If this information is missing, do not use the addressograph stamp; leave the fields blank
3. If additional continuous intravenous medications are ordered during the length-of-stay in CVICU, then transcribe the new medications if hemodynamic parameters are provided in the Doctors Orders sheets

VI. CARDIOVASCULAR INTENSIVE CARE STAY [Filename: AUDIT.WK3]

A. Post-operative Laboratory Results

1. Using the cumulative laboratory result sheets, record the following data for the entire length-of-stay in CVICU:
    a. WBC
    b. HGB
    c. HCT
    d. PLATELET CT
    e. PT
    f. PTT
    g. NA
    h. K
    i. CO2
    j. OSMO
    l. CREATININE
    m. GLUCOSE
    n. IONIZED CA
    o. CA
    p. PHOSPHATE
    q. MG
    r. CK
    s. TOTAL PROTEIN
    t. ALBUMIN
    u. BUN

Post-operative Laboratory Results Notes:

1. Transcribe numerical results to the same number of decimal places as shown on the cumulative sheets
2. Enter the date and time of the laboratory results as given on the cumulative sheets
3. Note in the TEXT column "Specimen hemolyzed" if so indicate on sheets

B. Post-operative Blood Gas Results

1. Record the following data according to the white blood gas forms for the entire length-of-stay in CVICU:
    a. Date and time of blood gas analysis.
    b. Ventilator Mode (if applicable)
    c. AC/SIMV rate (if applicable)
    d. PEEP (if applicable)
    e. FiO2 (if applicable)
    f. O2 SAT
    g. PO2
    h. PCO2
    i. H+
    j. PH
    k. SaO2
    l. Base Excess
    m. HCO3
    n. Temperature (øC)

C. Respiratory Therapy Ventilation Monitoring

1. Record the following data for the entire length-of-stay in CVICU:
    a. Date and time of assessment and ventilation changes.
    b. Mode
    c. SIMV rate
    d. Effective Vt
    e. Peak pressure
    f. PEEP
    g. FiO2
    h. SaO2
    i. Date and time of extubation

Respiratory Therapy Ventilation Monitoring Notes

1. Record all ventilator settings when entering Effective Vt and Peak Pressure
2. Transcribe in the TEXT column all hand-written notes that describe the

rationale for ventilator changes.

3. If there is a discrepancy between the respiratory therapy monitoring forms, nurses notes, blood gas requisitions, and flow sheets, then record the data found on the monitoring forms for all entries (regardless of the source) and note an explanation in the "TEXT" column

D. Intake and Output
  1. Record all intravenous solutions, nasogastric intake, cardiac output solutions, and oral intake with the volume provided during an one hour period transcribed on the hour
  2. Record all urine and chest tube output with the volume produced during an one hour period transcribed on the hour
  3. Record any blood products with administration time and amount (ml), according to the pre-set code list, as described in the nurses notes and CVICU flow sheet
  4. Record all Jackson Pratt, hemovac, and nasogastric drainage in the "OTHER" column and transcribe the type of drainage in the "TEXT" column

E. Continuous Intravenous Medications
  1. Record all continuous intravenous medications, according to the pre-set codelist, as described in the nurses notes and flow-sheet. Transcribe the medications on a minute-by-minute basis
  2. If provided, record the starting and finishing times for the continuous intravenous medications, according to the pre-set codelist
  3. If rate changes are inserted into the CVICU flowsheet but are not recorded in the nurses notes, transcribe the change to the nearest 15 minute interval and record the discrepancy in the "TEXT" column

F. Nurses Notes
  1. Record the surgical procedure and related diagnoses on the first line of the TEXT column
  2. Insert "WEIGHT" into TEXT column, record amount (kg) in the "WT" column according to the time given in the nurses notes
  3. Transcribe the following data:
    a. sponge bath, post-operative bath as "bedbath"
    b. chest x-ray
    c. turning, positioning, and back care as "re-positioned"
    d. chest physio
    e. all visitors as "family"
    f. zeroing and calibration of all central and arterial lines
    g. state of consciousness (eg. "restless", "agitated", "drowsy")
    h. elevation of the head of the bed by degrees
    i. warming and cooling interventions (eg. "warming blanket", "fan")
    j. pacemaker (only if turned on, do not record settings)
  4. If the text is indecipherable or ambiguous, consult the CVICU Clinical Nursing Unit supervisors for clarification
  5. If the patient returns to the OR, then record intra-operative and post-operative laboratory results, blood gas results, and hemodynamics. Transcribe the event in the "TEXT" column. Record the patient's return to CVICU

G. Medication Records
  1. Using the green medication record, transcribe all medications with administration times and dosages, according to the pre-set code list, that were given during the entire length-of-stay in CVICU.
  2. If there is a discrepancy between the medication records and the nurses notes, then use the time and dosage provided in the medication record. Note an explanation in the "TEXT" column

APPENDIX D – PROPOSED THERAPEUTIC PROTOCOLS FOR CVICU

Draft Version 1.5
October 9, 1992

1.0 Definitions for high and low values:

1.1 The common parameters used in the proposed protocols include: HR-heart rate, MAP-mean arterial pressure, CI-cardiac index, CVP-central venous pressure, PAD-pulmonary arterial diastolic, WP-wedge pressure, SVRI-systemic vascular resistance index, PVRI-pulmonary vascular resistance index, CT-chest tube loss, PT-prothrombine, PTT-partial thromboplastin.

1.2 Five parameters are used to form a hemodynamic pattern: HR, MAP, CI, PAD and CVP. Each pattern is labeled as an aberrancy and at least one specific therapeutic intervention can be defined for each aberrancy. Many of the aberrancies are actually gradations in severity of the same clinical problem. WP, when available, can be used to validate PAD. In the absence of pulmonary emboli, spasm, edema or high airway pressure, WP is equal to PAD.

1.3 The therapeutic ranges for MAP, PAD and CVP are defined by the clinician as deemed appropriate for each CV patient. Acceptable HR and CI are usually between 60-120 and 2.2-3.5, respectively. MAP, PAD and CVP ranges should be tight especially early on post-op. Specifically:

(a) early on, MAP should be around 10-15% below pre-op value, with the absolute low value not usually below 60 mmHg.

(b) CVP and PAD may need to be higher in the case of post-op cardiac dysfunction compared with pre-op value and with no cardiac dysfunction.

1.4 For example, for a patient with pre-op MAP of 95 and when leaving the O.R. with MAP of 85, a therapeutic MAP range of 75-90 would be acceptable. If the patient is bleeding, you may adjust MAP down to 70-80 for the next couple of hours. CVP and PAD may be set to 8-12.

1.5 Basic assessment is in 5 minutes interval, i.e. when MAP is low, it means over the last 5 minutes the median MAP is below acceptable therapeutic range. This is due to the limitation in the resolution of existing hemodynamic data obtained from the monitor, which is at one-minute intervals only.

1.6 When parameters are at warning-low or high levels, they are monitored over the next 10 minutes before any intervention is to take place.

1.7 When parameters are at alert-low or high levels, they are monitored over the next 5 minutes before any intervention is to take place.

1.8 When parameters are at critical-low or high levels, one would intervene immediately without any further monitoring.

1.9 The interventions for warning, alert and critical levels of a given clinical problem are usually the same, the difference is only in terms of timing as outlined above, e.g. with alert low MAP and CVP, the intervention is usually to give volume if condition persists over the next 5 minutes; but with critical low MAP and CVP one will give volume immediately.

2.0 Hypotension associated with absolute hypovolemia due to volume-depletion and/or bleeding:

```
2.1   if     MAP = low
      and    (CVP or WP or PAD) = low
      and    (CT >= 3 ml/kg/hr and CT < 5 ml/kg/hr for 3 hours) or (CT >= 5 ml/kg/hr)
      then
             condition = active bleeding, hypotension, absolute hypovolemia
             test = check for coagulopathy (see 2.2)
             therapy = give volume (includes blood products, see section 10.0)
             therapy = return to OR

2.2   if     test = check for coagulopathy
      and    condition = active-bleeding
      and    (PT-INR > 0.8) or (PTT > 40) or (platelets < 80000) or
             (D-dimer > 2) or (Euglobulin-lysis < 90)
      then
             condition = coagulopathy associated with bleeding
             therapy = treat-for-coagulopathy (see section 10.0)

2.3   if     MAP = low
      and    (CVP or WP or PAD) = low
      and    (HR = normal) or (HR = high and VPB < 5) or (HR = high and sinus-rhythm present)
      and    (CT >= 1 ml/hr and <  3 ml/kg/hr for 3 hours) or (CT >= 3 ml/kg/hr and < 5 ml/kg/hr)
      and    (clinical-findings = cool and clammy-extremities and weak-pulse)
      and    (URINE < 0.5 ml/kg/h) or (URINE >= 0.5 ml/kg/hr)
      and    (I/O-balance >= -1 litre) or (I/O-balance < -1 litre)
      and    trendelenburg-position not possible
      then
             condition = absolute-hypovolemia, hypotension, bleeding and/or oliguria
             test = check all catheter lines, cuff-pressures and recalibration
             test = check for coagulopathy
             therapy = give volume

2.4   if     MAP = low
      and    (CVP or WP or PAD) = low
      and    HR = normal or high
      and    CT < 1 ml/kg/hour
      and    (clinical-findings = cool and clammy-extremities and weak-pulse)
      and    (I/O-balance >= -1 litre) or (I/O-balance < -1 litre)
      and    (URINE < 0.5 ml/kg/hr) or (URINE >= 0.5 ml/kg/hr)
      and    trendelenburg-position not possible
      then
             condition = absolute-hypovolemia, hypotension and/or oliguria
             test = check all catheter lines, cuff-pressures and recalibration
             therapy = give volume
```

2.5 if MAP = low
and HR = low
and (CVP or PAD or WP) = normal or low
and atrial-wire in place
and CT < 1 ml/kg/hour
and (I/O-balance >= -1 litre) or (I/O-balance < -1 litre)
and (URINE < 0.5 ml/kg/hr) or (URINE >= 0.5 ml/kg/hr)
and trendelenburg-position not possible
then
condition = absolute-hypovolemia, hypotension, bradycardia
test = check all catheter lines, cuff-pressures and recalibration
therapy = atrial pacing

2.6 if MAP = low
and HR = low
and (CVP or WP or PAD) = low
and atrial-wire not in place
and CT < 1 ml/kg/hour
and (I/O-balance >= -1 litre) or (I/O-balance < -1 litre)
and (URINE < 0.5 ml/kg/hr) or (URINE >= 0.5 ml/kg/hr)
and (preop-medication = negative-chronotrope) or
(diagnosis = heart-block or sinus-node-dysfunction or others)
and trendelenburg-position not possible
then
condition = absolute-hypovolemia, hypotension, bradycardia
test = check all catheter lines, cuff-pressures and recalibration
therapy = give volume

2.7 if MAP = low
and HR = low
and (CVP or WP or PAD) = low
and atrial-wire not in place
and CT < 1 ml/kg/hour
and (I/O-balance >= -1 litre) or (I/O-balance < -1 litre)
and (URINE < 0.5 ml/kg/hr) or (URINE >= 0.5 ml/kg/hr)
and (preop-medication = negative-chronotrope) or
(diagnosis = heart-block or sinus-node-dysfunction)
and volume-therapy failed
and trendelenburg-position not possible
then
condition = absolute-hypovolemia, hypotension, bradycardia
therapy = give chronotrope

```
2.8     if      MAP = low
        and     (CVP or WP or PAD) = low
        and     HR = low
        and     CT < 1 ml/kg/hour
        and     (I/O-balance >= -1 litre) or (I/O-balance < -1 litre)
        and     (URINE < 0.5 ml/kg/hr) or (URINE >= 0.5 ml/kg/hr)
        and     atrial-wire not in place
        and     volume-therapy failed
        and     chronotrope-therapy failed
        and     trendelenburg-position not possible
        then
                condition = absolute-hypovolemia, hypotension, bradycardia
                test = check all catheter lines, cuff-pressures and recalibration
                test = do EKG diagnosis
                therapy =  turn ventricular-pacer on and/or pacing swan catheter


2.9     if      MAP = low
        and     HR = high
        and     (CVP or WP or PAD = low or normal)
        and     (CI = low) or
                (Base or CO2 or pCO2 or H = abnormal) or
                (mixed venous O2 Saturation = low)
        and     CT < 1 ml/kg/hour
        and     (I/O-balance >= -1 litre) or (I/O-balance < -1 litre)
        and     (URINE < 0.5 ml/kg/hr) or (URINE >= 0.5 ml/kg/hr)
        and     > 10 ug/kg/min nipride for at least 3 hours
        and     clinical-findings = no muscle rigidity
        and     trendelenburg-position not possible
        then
                condition = suspected cyanide toxicity
                test = serum thiocyanide level
                therapy = stop nipride therapy
                therapy = sodium thiosulfate
```

3.0 Interpretation of Trendelenburg test when MAP = low and (CVP or WP or PAD) = low

```
3.1    if      test = trendelenburg position for 3 minutes
       and     HR = low or normal or high
       and     (MAP increases >= 10%) and (MAP = low)
       and     (CVP or PAD or WP increases >= 10% and = low) or
               (CVP or PAD or WP stays the same and = low)
       and     CT < 1 ml/kg/hour
       and     (I/O-balance >= -1 litre) or (I/O-balance < -1 litre)
       and     (URINE < 0.5 ml/kg/hr) or (URINE >= 0.5 ml/kg/hr)
       and     vasodilator not present
       then
               condition = hypotension, absolute hypovolemia
               therapy = give volume

3.2    if      test = trendelenburg position for 3 minutes
       and     HR = low or normal or high
       and     (MAP increases >= 10%) and (MAP = normal)
       and     (CVP or PAD or WP increases >= 10% and = normal) or
               (CVP or PAD or WP stays the same and = normal)
       and     CT < 1 ml/kg/hour
       and     (I/O-balance >= -1 litre) or (I/O-balance < -1 litre)
       and     (URINE < 0.5 ml/kg/hr) or (URINE >= 0.5 ml/kg/hr)
       and     vasodilator not present
       then
               condition = compensated hypotension and hypovolemia
               therapy = none required

3.3    if      test = trendelenburg position for 3 minutes
       and     HR = normal or high
       and     (MAP stays the same or decreased) and (MAP = low)
       and     (CVP or PAD or WP increases >= 10% and = low)
       and     CT < 1 ml/kg/hour
       and     (I/O-balance >= -1 litre) or (I/O-balance < -1 litre)
       and     (URINE < 0.5 ml/kg/hr) or (URINE >= 0.5 ml/kg/hr)
       then
               condition = ventricular-dysfunction, hypotension, absolute-hypovolemia
               test = check for tamponade
               therapy = give inotrope for cardiac dysfunction or
               therapy = strip chest-tube, open chest in ICU or OR if tamponade
```

3.4 if test = trendelenburg position for 3 minutes
and HR = low
and (MAP stays the same or decreased) and (MAP = low)
and (CVP or PAD or WP increases >= 10% and = low) or
(CVP or PAD or WP stays the same and = low)
and CT < 1 ml/kg/hour
and (I/O-balance >= -1 litre) or (I/O-balance < -1 litre)
and (preop-medication = negative-chronotrope) or
(diagnosis = heart-block or sinus-node-dysfunction or others)
and (URINE < 0.5 ml/kg/hr) or (URINE >= 0.5 ml/kg/hr) or
(BASE or pCO2 or CO2 = abnormal)
then
condition = bradycardia, hypotension, absolute-hypovolemia and/or acidosis
therapy = give chronotrope

3.5 if test = trendelenburg position for 3 minutes
and (MAP increases >= 10%) and (MAP = low or normal)
and (CVP or PAD or WP increases >= 10%) and (CVP or PAD or WP = low or normal) or
(CVP or PAD or WP stays the same) and (CVP or PAD or WP = low or normal)
and HR = normal or high
and CT < 1 ml/kg/hour
and (I/O-balance >= -1 litre) or (I/O-balance < -1 litre)
and (URINE < 0.5 ml/kg/hr) or (URINE >= 0.5 ml/kg/hr)
and therapy = vasodilator
and (CI = low) or (BASE or CO2 or H or pCO2 or K or Ca or IonCa = abnormal)
then
condition = hypovolemia, acidosis, hypotension
therapy = give volume

3.6 if test = trendelenburg position for 3 minutes
and (MAP increases >= 10%) and (MAP = low or normal)
and (CVP or PAD or WP increases >= 10%) and (CVP or PAD or WP = low or normal) or
(CVP or PAD or WP stays the same) and (CVP or PAD or WP = low or normal)
and HR = normal or high
and CT < 1 ml/kg/hour
and (I/O-balance >= -1 litre) or (I/O-balance < -1 litre)
and (URINE < 0.5 ml/kg/hr) or (URINE >= 0.5 ml/kg/hr)
and therapy = vasodilator
and (CI = normal) or (BASE and CO2 and H and pCO2 and K and Ca and IonCa = normal)
then
condition = hypovolemia, acidosis, hypotension
therapy = reduce vasodilator

4.0 Hypotension induced-by relative hypovolemia due to arterial vasodilation:

```
4.1   if     MAP = low
      and    (CVP or WP or PAD) = high or normal
      and    HR = normal or high
      and    SVRI = low or normal
      and    PVRI = normal
      and    CI = normal or high
      and    (K and Ca  and pCO2 and CO2 and Base and H = normal)
      and    clinical-findings = warm extremities and bounding pulse
      and    URINE > 0.5 ml/kg/hour
      and    vasodilators = present
      then
             condition = relative-hypovolemia, hypotension, normal cardiac function
             test = check all catheter lines, cuff-pressures and recalibration
             therapy = reduce vasodilator

4.2   if     MAP = low
      and    (CVP or WP or PAD) = high or normal
      and    HR = normal or high
      and    URINE > 0.5 ml/kg/hour
      and    vasodilators = present
      and    (K and Ca  and pCO2 and CO2 and Base and H = normal)
      and    (clinical-findings = warm extremities and bounding pulse)
      then
             condition = relative-hypovolemia, hypotension, normal cardiac function
             test = check all catheter lines, cuff-pressures and recalibration
             therapy = reduce vasodilator

4.3   if     MAP = low
      and    (CVP or WP or PAD) = high
      and    HR = normal or high
      and    SVRI = low or normal
      and    PVRI = normal
      and    CI = normal or high
      and    (K and Ca  and pCO2 and CO2 and Base and H = normal)
      and    clinical-findings = warm extremities and bounding pulse
      and    URINE > 0.5 ml/kg/hr
      and    temperature > 38.0
      then
             condition = hypotension, normal cardiac function, pyrexia
             test = check all catheter lines, cuff-pressures and recalibration, trendelenburg-position
             therapy = give vasoconstrictor
             therapy = active cooling of temperature
```

4.4 if MAP = low
and (CVP or WP or PAD) = normal
and HR = normal or high
and SVRI = low or normal
and PVRI = normal
and CI = normal or high
and (K and Ca and pCO2 and CO2 and Base and H = normal)
and clinical-findings = warm extremities and bounding pulse
and URINE > 0.5 ml/kg/hr
and temperature > 38.0
then

condition = hypotension, normal cardiac function, pyrexia
test = check all catheter lines, cuff-pressures and recalibration, trendelenburg-position
therapy = give vasoconstrictor
therapy = active cooling of temperature
therapy = give volume

4.5 if MAP = low
and (CVP or WP or PAD) = high or normal
and HR = normal or high
and SVRI = low or normal
and PVRI = normal
and CI = normal or high
and (K and Ca and pCO2 and CO2 and Base and H = normal)
and clinical-findings = warm extremities and bounding pulse
and URINE > 0.5 ml/kg/hr
and temperature > 38.0
and vasodilator present
then

condition = relative-hypovolemia, hypotension, normal cardiac function, pyrexia
test = check all catheter lines, cuff-pressures and recalibration, trendelenburg-position
therapy = reduce vasodilator
therapy = active cooling of temperature

4.6 if MAP = low
and (CVP or WP or PAD) = high or normal
and HR = normal or high
and temperature > 38.0
and (WBC > 10) or (LOS > 3 days) or
(intravascular lines > 48 hours) or (condition = respiratory or urinary infection)
then

condition = hypotension, pyrexia, sepsis
test = check all catheter lines, cuff-pressures and recalibration
therapy = active cooling of temperature
therapy = give antibiotics

```
4.7    if      MAP = low
       and     (CVP or WP or PAD) = high
       and     HR = normal or high
       and     vasodilators = present
       and     (K or Ca  or pCO2 or CO2 or Base or H = abnormal)  or
               (SVRI = normal or high) or (PVRI = normal or high) or (CI = low)
       then
               condition = hypotension, cardiac dysfunction
               test = check all catheter lines, cuff-pressures and recalibration
               therapy = give inotrope


4.8    if      MAP = low
       and     (CVP or WP or PAD) = normal
       and     HR = normal or high
       and     vasodilators = present
       and     (K or Ca  or pCO2 or CO2 or Base or H = abnormal)  or
               (SVRI = normal or high) or (PVRI = normal or high) or (CI = low)
       then
               condition = hypotension, cardiac dysfunction
               test = check all catheter lines, cuff-pressures and recalibration, trendelenburg-position
               therapy = give inotrope
               therapy = give volume
```

9.0 Responses to therapy:

```
9.1     if      therapy = give volume
        and     agent = crystalloid for at least 15 minutes
        and     MAP change after volume therapy < 10% and MAP = low
        and     (CVP or WP or PAD change after volume therapy < 10% and = low) or
                (no CVP and WP and PAD present)
        and     URINE change after volume therapy < 10%
        then
                condition = crystalloid-therapy inadequate
                therapy = repeat crystalloid-therapy


9.2     if      therapy = give volume
        and     agent = colloid for at least 15 minutes
        and     MAP change after volume therapy < 10% and MAP = low
        and     (CVP or PW or PAD change after volume therapy < 10% and = low) or
                (no CVP and WP and PAD present)
        and     URINE change after volume therapy < 10%
        then
                condition = colloid-therapy inadequate
                therapy = repeat colloid-therapy


9.3     if      therapy = give volume
        and     agent = volume for at least 15 minutes
        and     MAP = normal
        and     (CVP or WP or PAD) = normal
        and     HR = low or normal or (HR = high and sinus-rhythm present)
        and     CT < 1 ml/kg/hour
        and     (I/O-balance >= -1 litre) or (I/O-balance < -1 litre)
        and     (URINE >= 0.5 ml/kg/hr)
        then
                condition = volume-therapy successful
```

10.0 Volume Resuscitation Protocols

```
10.1   if     therapy = give volume
       and    (HCT within last 12 hours < 27 and HCT within last 12 hours >= 24) or
              (Hb within last 12 hours < 9 and Hb within last 12 hours >= 8)
       and    ICU-admission since surgery < 5 hours
       and    autotransfusion-system available
       then
              agent = autotransfusion

10.2   if     therapy = give volume
       and    (HCT within last 12 hours < 24) or (Hb within last 12 hours < 8)
       and    ICU-admission since surgery < 5 hours
       and    autotransfusion-system available
       then
              agent = autotransfusion

10.3   if     therapy = give volume
       and    (HCT within last 12 hours < 27 and HCT within last 12 hours >= 24) or
              (Hb within last 12 hours < 9 and Hb within last 12 hours >= 8)
       and    ICU-admission since surgery >= 5 hours
       and    autotransfusion-system not available
       then
              agent = crystalloid or colloid

10.4   if     therapy = give volume
       and    (HCT within last 12 hours < 24) or (Hb within last 12 hours < 8)
       and    ICU-admission since surgery >= 5 hours
       and    autotransfusion-system not available
       then
              agent = packed-cells

10.5   if     therapy = give volume
       and    OSM within last 6 hours < 280
       and    weight-gain > 10% admission-weight
       and    condition is not ARDS and COPD
       and    clinical-findings = peripheral edema
       and    (URINE >= 1 ml/kg/hour) or (URINE < 1 ml/kg/hour)
       and    (I/O-balance < -1 litre) or (I/O-balance >= -1 litre)
       then
              agent = 25% albumin

10.6   if     therapy = give volume
       and    condition is ARDS or COPD
       and    HCT within last 12 hours < 40
       then
              agent = packed cells
```

```
10.7   if     therapy = give volume
       and    (OSM within last 6 hours >= 280) and (OSM within last 6 hours <= 300)
       and    weight-gain < 10% admission-weight
       and    (serum Na within last 6 hours >= 135) and (serum Na within last 6 hours <= 150)
       and    (URINE >= 1 ml/kg/hour) or (URINE < 1 ml/kg/hour)
       and    (I/O-balance < -1 litre) or (I/O-balance >= -1 litre)
       and    condition is not ARDS and COPD
       and    crystalloid-therapy not failed
       then
              agent = ringers lactate or normal saline


10.8   if     therapy = give volume
       and    (OSM within last 6 hours > 300) or (OSM within last 6 hours < 300)
       and    weight-gain < 10% admission-weight
       and    serum Na within last 6 hours > 150
       and    condition is not ARDS and COPD
       and    crystalloid-therapy not failed
       then
              agent = D5W


10.9   if     therapy = give volume
       and    OSM within last 6 hours > 300
       and    weight-gain < 10% admission-weight
       and    serum Na within last 6 hours < 135
       and    condition is not ARDS and COPD
       and    crystalloid-therapy not failed
       then
              agent = normal saline or lactate ringers


10.10  if     therapy = give volume
       and    OSM within last 6 hours < 295
       and    serum Na within last 6 hours < 150
       and    condition is not ARDS and COPD
       and    clinical-findings = edema or
              (weight-gain > 10% admission-weight) or
       then
              agent = 25% albumin


10.11  if     therapy = give volume
       and    (OSM within last 6 hours >= 295) and (OSM within last 6 hours < 300)
       and    serum Na within last 6 hours < 150
       and    condition is not ARDS and COPD
       and    clinical-findings = edema or
              (weight-gain > 10% admission-weight) or
       then
              agent = 5% albumin
```

10.12 if condition = active-bleeding
and PT-INR > 1.8
and therapy = treat for coagulopathy
then

agent = fresh-frozen-plasma

10.13 if condition = active-bleeding
and PT-INR > 1.8 and PTT > 40
and fibrinogen < 1.5
then

agent = cryoprecipitate

10.13 if condition = active-bleeding
and PTT > 40
and therapy = treat for coagulopathy
then

agent = protamine 50 mg

10.14 if condition = active-bleeding
and platelets < 40,000
and therapy = treat for coagulopathy
then

agent = platelets

10.15 if condition = active-bleeding
and (diagnosis = liver dysfunction) or (pre-op medication = coumadin)
and therapy = treat for coagulopathy
then

agent = fresh-frozen-plasma and vitamin-K1

10.16 if condition = active-bleeding
and (diagnosis = fibrinolysis) or (D-dimer > 2) or (euglobin-lysis < 90)
and fibrinogen = normal
and therapy = treat for coagulopathy
then

agent = amicar

10.17 if condition = active-bleeding
and (diagnosis = fibrinolysis) or (D-dimer > 2) or (euglobin-lysis < 90)
and fibrinogen = low
and therapy = treat for coagulopathy
then

agent = amicar and cryoprecipitate

APPENDIX E – EMPIRICAL DRUG-DOSAGE RESPONSE TABLES

THERAPY	DOSAGE	HR	APS	MAP	APD	SVRI	PAS	PAM	PAD	PVRI	CVP	WP	CI	SI	URINE
INOTROPE															
- Isuprel															
low	<0.1ug/kg/min	2	0	1	-1	-1	1	1	1	-1	-1	-1	1	1	0
medium	0.1-0.5ug/kg/min	3	1	1	1	-2	1	1	1	-1	-1	-1	2	2	-1
high	>0.5ug/kg/min	3	1	1	1	-2	2	2	2	-2	-2	-2	3	3	-2
- Dobutamine															
very-low	0.5-5ug/kg/min	0	0	-1	-1	-1	0	0	0	0	0	0	1	1	0
low	6-10ug/kg/min	0	0	-1	0	-1	0	0	0	0	0	-1	2	2	1
medium	11-20ug/kg/min	1	1	1	1	1	1	1	1	1	-1	-2	3	3	2
high	>20ug/kg/min	1	2	2	2	2	2	2	2	2	-2	-2	3	3	2
- Dopamine															
very-low	0.5-5ug/kg/min	1	0	0	0	0	0	0	0	0	0	0	1	1	1
low	6-10ug/kg/min	1	1	1	1	1	0	0	0	0	1	1	2	2	2
medium	11-20ug/kg/min	2	2	2	2	2	1	1	1	1	2	2	3	3	2
high	>20ug/kg/min	3	3	3	3	3	2	2	2	2	2	2	2	2	1
- Epinephrine															
very-low	<0.04ug/kg/min	1	0	0	-1	0	0	0	0	0	0	0	1	0	-1
low	0.04-0.08ug/kg/min	2	0	1	1	1	0	0	0	0	1	1	2	1	-1
medium	0.09-0.2ug/kg/min	2	1	1	1	2	1	1	1	1	2	2	2	2	-2
high	>0.2ug/kg/min	3	2	2	2	3	2	2	2	2	3	3	2	2	-3
- Norepinephrine															
very-low	<0.04ug/kg/min	0	1	1	1	1	1	1	0	0	1	1	0	0	-1
low	0.04-0.08ug/kg/min	0	2	2	1	2	2	2	1	1	3	2	0	0	-2
medium	0.09-0.2ug/kg/min	1	3	3	2	3	2	2	2	2	3	2	-1	-1	-3
high	>0.2ug/kg/min	2	3	3	3	3	3	3	3	3	3	3	1	1	-3
Phos.Inhibitor															
- Amrinone															
low	<5ug/kg/min	0	0	0	0	-1	0	0	0	-1	0	0	1	1	0
medium	5-15ug/kg/min	1	-1	-1	-1	-2	-1	-1	-1	-2	-1	-1	2	2	1
high	>15ug/kg/min	2	-2	-2	-2	-2	-2	-2	-2	-2	-1	-2	2	2	1
- Digoxin															
low	1ug/kg/day	-1	0	0	0	0	0	0	0	0	0	0	1	1	0
medium	2-4ug/kg/day	-2	0	0	0	0	0	0	0	0	0	0	1	2	0
high	5ug/kg/day	-3	0	0	0	0	0	0	0	0	0	0	1	3	0
CHRONOTROPE															
Anagonist															
- Verapamil	0.05ug/kg or 3mg	-1	-1	-1	-1	0	-1	-1	-1	0	0	-1	-1	-1	0
	0.1ug/kg or 7mg	-2	-2	-2	-2	0	-2	-2	-2	0	0	-2	-2	-2	0
- Edrophonium	0.2ug/kg	-1	0	0	0	0	0	0	0	0	0	0	-1	-1	0
	0.5ug/kg	-2	0	0	0	0	0	0	0	0	0	0	-1	-1	0
	1.0ug/kg	-3	0	0	0	0	0	0	0	0	0	0	-1	-1	0
- Atropine	20ug/kg	2	1	1	1	0	0	0	0	0	-1	-1	1	1	0
	40ug/kg	3	1	1	1	0	-1	-1	-1	0	-1	-1	1	1	0
- Propranolol	0.01ug/kg 0.5mg	-1	0	0	0	0	0	0	0	0	0	0	0	0	0
	0.05ug/kg	-2	-1	-1	-1	1	1	1	1	1	1	1	-1	-1	0
- Labetalol	alpha														
	beta														
low	<0.02ug/kg/min	-1	0	0	0	-1	0	0	0	0	0	0	-1	-1	0
medium	.02-.06ug/kg/min	-2	-1	-1	-1	-2	-1	-1	-1	-1	0	0	-2	-2	0
high	>0.06ug/kg/min	-3	-2	-2	-2	-2	-1	-1	-1	-1	-1	-1	-2	-2	0
VASOTROPE															
- Nipride															
low	<1ug/kg/min	0	-1	-1	-1	-1	0	-1	-1	0	-1	-1	1	1	0
medium	1-4ug/kg/min	1	-2	-2	-2	-2	-1	-1	-1	-1	-2	-2	2	2	0
high	>4ug/kg/min	1	-3	-3	-3	-3	-1	-1	-1	-1	-2	-3	2	2	0
- Nitroglycerine															
low	<1ug/kg/min	0	0	0	0	-1	0	0	0	0	-1	-1	1	1	0
medium	1-4ug/kg/min	0	-1	-1	-1	-2	-1	-1	-1	-1	-2	-2	2	2	0
high	>4ug/kg/min	1	-2	-2	-2	-2	-2	-2	-2	-2	-3	-3	2	2	0
- Nifedipine	SL 0.15mg/kg														
- Phenylephrine															
low	0.04-0.08ug/kg/min	-1	1	2	1	2	0	0	0	0	1	1	-1	0	0
medium	0.09-0.2ug/kg/min	-1	2	3	2	3	1	1	1	1	1	1	-1	-1	-1
high	>0.2ug/kg/min	-2	3	3	3	3	1	1	1	1	2	2	-2	-2	-2
ECFV															
- Lasix															
low	<1ug/kg/min	0													
medium	1-2ug/kg/min	0													
high	>2ug/kg/min	0													
- Crystolloids	4 to 1 effect as colloid														
- Albumin 5%	if depleted	-1	1	1	1						1	1	1	1	1
	if not depleted										2	2	0	0	

APPENDIX F - COMPUTATIONAL DRUG-DOSAGE RESPONSE TABLES

THERAPY INOTROPE	DOSAGE	conc	log	HR	ABPS	APM	ABPD	SVRI	PAPS	PAPM	PAPD	PVRI	CVP	WP	CI	SI	URINE
- Isuprel low	<0.1ug/kg/min	1	0.00	0.16		0.05	-0.05	-0.05	0.05	0.05	0.05	-0.1	-0.1	-0.1	0.05	0.05	
	<5ug/min	2	0.30	0.20		0.07	-0.01	-0.08	0.08	0.08	0.08	-0.08	-0.08	-0.08	0.08	0.08	
		4	0.60	0.23		0.09	0.03	-0.10	0.10	0.10	0.10	-0.10	-0.10	-0.10	0.10	0.10	
medium	0.1-0.5ug/kg/min	6	0.78	0.25		0.10	0.05	-0.12	0.12	0.12	0.12	-0.12	-0.12	-0.12	0.12	0.12	
		8	0.90	0.27		0.11	0.07	-0.13	0.13	0.13	0.13	-0.13	-0.13	-0.13	0.13	0.13	
		10	1.00	0.28		0.11	0.08	-0.13	0.13	0.13	0.13	-0.13	-0.13	-0.13	0.13	0.13	
		15	1.18	0.3		0.13	0.10	-0.15	0.15	0.15	0.15	-0.15	-0.15	-0.15	0.15	0.15	
		20	1.30	0.35	0.05	0.13	0.12	-0.2	0.16	0.16	0.16	-0.16	-0.16	-0.16	0.16	0.16	-0.05
		25	1.40	0.39	0.09	0.14	0.13	-0.22	0.22	0.22	0.22	-0.22	-0.22	-0.22	0.28	0.28	-0.15
high	>0.5ug/kg/min	30	1.48	0.42	0.12	0.15	0.14	-0.26	0.26	0.26	0.26	-0.26	-0.26	-0.26	0.37	0.37	-0.23
		35	1.54	0.45	0.15	0.15	0.15	-0.30	0.30	0.30	0.30	-0.30	-0.30	-0.30	0.45	0.45	-0.30
- Dobutamine very-low	0.5-5ug/kg/min	0	0.00			0.00	0.00	0.00									
		0.25	0.00			0.00	0.00	0.00									
		0.5	0.00			0.00	0.00	0.00									
		1	0.00			0.00	0.00	0.00									
		2	0.30			-0.06	-0.09	-0.06							0.06	0.06	
		3	0.48			-0.09	-0.15	-0.09							0.09	0.09	
		4	0.60			-0.12	-0.09	-0.12							0.12	0.12	
		5	0.70			-0.13	-0.04	-0.13							0.13	0.13	
low	6-10ug/kg/min	6	0.78			-0.15	0.00	-0.15							0.15	0.15	0.05
		7	0.85			-0.10	0.01	-0.10							0.17	0.17	0.07
		8	0.90			-0.06	0.02	-0.06							0.20	0.20	0.10
		9	0.95			-0.02	0.03	-0.02							0.21	0.21	0.11
		10	1.00			0.02	0.04	0.02							0.23	0.23	0.13
medium	11-20ug/kg/min	11	1.04	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	-0.05	-0.15	0.25	0.25	0.15
		12	1.08	0.06	0.07	0.07	0.07	0.07	0.07	0.07	0.07	0.07	-0.07	-0.16	0.26	0.26	0.16
		13	1.11	0.06	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08	-0.08	-0.17	0.27	0.27	0.17
		14	1.15	0.07	0.10	0.10	0.10	0.10	0.10	0.10	0.10	0.10	-0.10	-0.18	0.28	0.28	0.18
		15	1.18	0.07	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11	-0.11	-0.19	0.29	0.29	0.19
		16	1.20	0.08	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12	-0.12	-0.19	0.31	0.31	0.21
		17	1.23	0.08	0.13	0.13	0.13	0.13	0.13	0.13	0.13	0.13	-0.13	-0.20	0.31	0.31	0.21
		18	1.26	0.09	0.15	0.15	0.15	0.15	0.15	0.15	0.15	0.15	-0.15	-0.21	0.32	0.32	0.22
		19	1.28	0.09	0.16	0.16	0.16	0.16	0.16	0.16	0.16	0.16	-0.16	-0.21	0.33	0.33	0.23
		20	1.30	0.10	0.17	0.17	0.17	0.17	0.17	0.17	0.17	0.17	-0.17	-0.22	0.34	0.34	0.24
high	>20ug/kg/min	21	1.32	0.10	0.18	0.18	0.18	0.18	0.18	0.18	0.18	0.18	-0.18	-0.23	0.35	0.35	0.25
		22	1.34	0.10	0.18	0.18	0.18	0.18	0.18	0.18	0.18	0.18	-0.18	-0.23	0.36	0.36	0.26
		23	1.36	0.11	0.19	0.19	0.19	0.19	0.19	0.19	0.19	0.19	-0.19	-0.24	0.36	0.36	0.26
		24	1.38	0.11	0.20	0.20	0.20	0.20	0.20	0.20	0.20	0.20	-0.20	-0.24	0.37	0.37	0.27
		25	1.40	0.11	0.21	0.21	0.21	0.21	0.21	0.21	0.21	0.21	-0.21	-0.25	0.38	0.38	0.28
		26	1.41	0.12	0.22	0.22	0.22	0.22	0.22	0.22	0.22	0.22	-0.22	-0.25	0.38	0.38	0.28
		27	1.43	0.12	0.22	0.22	0.22	0.22	0.22	0.22	0.22	0.22	-0.22	-0.25	0.39	0.39	0.29
		28	1.45	0.12	0.23	0.23	0.23	0.23	0.23	0.23	0.23	0.23	-0.23	-0.26	0.39	0.39	0.29
		29	1.46	0.13	0.24	0.24	0.24	0.24	0.24	0.24	0.24	0.24	-0.24	-0.26	0.40	0.40	0.30
		30	1.48	0.13	0.24	0.24	0.24	0.24	0.24	0.24	0.24	0.24	-0.24	-0.27	0.40	0.40	0.30
		31	1.49	0.13	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	-0.25	-0.27	0.41	0.41	0.31
		32	1.51	0.13	0.26	0.26	0.26	0.26	0.26	0.26	0.26	0.26	-0.26	-0.27	0.41	0.41	0.31
		33	1.52	0.14	0.26	0.26	0.26	0.26	0.26	0.26	0.26	0.26	-0.26	-0.28	0.42	0.42	0.32
		34	1.53	0.14	0.27	0.27	0.27	0.27	0.27	0.27	0.27	0.27	-0.27	-0.28	0.42	0.42	0.32
		35	1.54	0.14	0.27	0.27	0.27	0.27	0.27	0.27	0.27	0.27	-0.27	-0.28	0.43	0.43	0.33
		36	1.56	0.14	0.28	0.28	0.28	0.28	0.28	0.28	0.28	0.28	-0.28	-0.29	0.43	0.43	0.33
		37	1.57	0.14	0.28	0.28	0.28	0.28	0.28	0.28	0.28	0.28	-0.28	-0.29	0.44	0.44	0.34
		38	1.58	0.15	0.29	0.29	0.29	0.29	0.29	0.29	0.29	0.29	-0.29	-0.29	0.44	0.44	0.34
		39	1.59	0.15	0.30	0.30	0.30	0.30	0.30	0.30	0.30	0.30	-0.30	-0.30	0.45	0.45	0.35
		40	1.60	0.15	0.30	0.30	0.30	0.30	0.30	0.30	0.30	0.30	-0.30	-0.30	0.45	0.45	0.30
- Dopamine very-low	0.5-5ug/kg/min	1	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
		2	0.30	0.05	0.02	0.02	0.02	0.02	0.01	0.01	0.01	0.01	0.02	0.02	0.06	0.06	0.06
		3	0.48	0.07	0.03	0.03	0.03	0.03	0.02	0.02	0.02	0.02	0.03	0.03	0.10	0.10	0.10
		4	0.60	0.09	0.04	0.04	0.04	0.04	0.03	0.03	0.03	0.03	0.04	0.04	0.12	0.12	0.12
		5	0.70	0.10	0.04	0.04	0.04	0.04	0.03	0.03	0.03	0.03	0.04	0.04	0.14	0.14	0.14
low	6-10ug/kg/min	6	0.78	0.12	0.05	0.05	0.05	0.05	0.04	0.04	0.04	0.04	0.05	0.05	0.16	0.16	0.16
		7	0.85	0.13	0.08	0.08	0.08	0.08	0.04	0.04	0.04	0.04	0.08	0.08	0.18	0.18	0.18
		8	0.90	0.14	0.11	0.11	0.11	0.11	0.04	0.04	0.04	0.04	0.11	0.11	0.20	0.20	0.20
		9	0.95	0.14	0.13	0.13	0.13	0.13	0.05	0.05	0.05	0.05	0.13	0.13	0.21	0.21	0.22
		10	1.00	0.15	0.15	0.15	0.15	0.15	0.05	0.05	0.05	0.05	0.15	0.15	0.22	0.22	0.24
medium	11-20ug/kg/min	11	1.04	0.16	0.16	0.16	0.16	0.16	0.05	0.05	0.05	0.05	0.16	0.16	0.24	0.24	0.25
		12	1.08	0.18	0.18	0.18	0.18	0.18	0.06	0.06	0.06	0.06	0.17	0.17	0.25	0.25	0.27
		13	1.11	0.19	0.19	0.19	0.19	0.19	0.08	0.08	0.08	0.08	0.18	0.18	0.26	0.26	0.28
		14	1.15	0.21	0.21	0.21	0.21	0.21	0.09	0.09	0.09	0.09	0.18	0.18	0.27	0.27	0.29
		15	1.18	0.22	0.22	0.22	0.22	0.22	0.10	0.10	0.10	0.10	0.19	0.19	0.27	0.27	0.30
		16	1.20	0.23	0.23	0.23	0.23	0.23	0.11	0.11	0.11	0.11	0.19	0.19	0.28	0.28	0.27
		17	1.23	0.24	0.24	0.24	0.24	0.24	0.12	0.12	0.12	0.12	0.20	0.20	0.29	0.29	0.24
		18	1.26	0.25	0.25	0.25	0.25	0.25	0.13	0.13	0.13	0.13	0.21	0.21	0.30	0.30	0.21

THERAPY	DOSAGE	conc	log	HR	ABPS	APM	ABPD	SVRI	PAPS	PAPM	PAPD	PVRI	CVP	WP	CI	SI	URINE
		19	1.28	0.26	0.26	0.26	0.26	0.26	0.14	0.14	0.14	0.14	0.21	0.21	0.30	0.30	0.18
		20	1.30	0.27	0.27	0.27	0.27	0.27	0.15	0.15	0.15	0.15	0.22	0.22	0.31	0.31	0.16
high	>20ug/kg/min	21	1.32	0.28	0.28	0.28	0.28	0.28	0.16	0.16	0.16	0.16	0.22	0.22	0.30	0.30	0.15
		22	1.34	0.29	0.29	0.29	0.29	0.29	0.16	0.16	0.16	0.16	0.22	0.22	0.29	0.29	0.14
		23	1.36	0.30	0.30	0.30	0.30	0.30	0.17	0.17	0.17	0.17	0.23	0.23	0.29	0.29	0.14
		24	1.38	0.31	0.31	0.31	0.31	0.31	0.18	0.18	0.18	0.18	0.23	0.23	0.28	0.28	0.13
		25	1.40	0.32	0.32	0.32	0.32	0.32	0.19	0.19	0.19	0.19	0.24	0.24	0.27	0.27	0.13
		26	1.41	0.32	0.32	0.32	0.32	0.32	0.19	0.19	0.19	0.19	0.24	0.24	0.27	0.27	0.13
		27	1.43	0.33	0.33	0.33	0.33	0.33	0.20	0.20	0.20	0.20	0.24	0.24	0.26	0.26	0.12
		28	1.45	0.34	0.34	0.34	0.34	0.34	0.20	0.20	0.20	0.20	0.25	0.25	0.25	0.25	0.12
		29	1.46	0.35	0.35	0.35	0.35	0.35	0.21	0.21	0.21	0.21	0.25	0.25	0.25	0.25	0.11
		30	1.48	0.35	0.35	0.35	0.35	0.35	0.22	0.22	0.22	0.22	0.25	0.25	0.24	0.24	0.11
		31	1.49	0.36	0.36	0.36	0.36	0.36	0.22	0.22	0.22	0.22	0.26	0.26	0.24	0.24	0.11
		32	1.51	0.36	0.36	0.36	0.36	0.36	0.23	0.23	0.23	0.23	0.26	0.26	0.23	0.23	0.10
		33	1.52	0.37	0.37	0.37	0.37	0.37	0.23	0.23	0.23	0.23	0.26	0.26	0.23	0.23	0.10
		34	1.53	0.38	0.38	0.38	0.38	0.38	0.24	0.24	0.24	0.24	0.26	0.26	0.22	0.22	0.09
		35	1.54	0.38	0.38	0.38	0.38	0.38	0.24	0.24	0.24	0.24	0.27	0.27	0.22	0.22	0.09
		36	1.56	0.39	0.39	0.39	0.39	0.39	0.25	0.25	0.25	0.25	0.27	0.27	0.21	0.21	0.09
		37	1.57	0.39	0.39	0.39	0.39	0.39	0.25	0.25	0.25	0.25	0.27	0.27	0.21	0.21	0.08
		38	1.58	0.40	0.39	0.39	0.39	0.40	0.25	0.25	0.25	0.25	0.27	0.27	0.20	0.20	0.08
		39	1.59	0.40	0.39	0.39	0.39	0.40	0.26	0.26	0.26	0.26	0.28	0.28	0.20	0.20	0.08
		40	1.60	0.41	0.39	0.39	0.39	0.41	0.26	0.26	0.26	0.26	0.28	0.28	0.20	0.20	0.08
		41	1.61	0.41	0.40	0.40	0.40	0.41	0.27	0.27	0.27	0.27	0.28	0.28	0.19	0.19	0.07
		42	1.62	0.42	0.40	0.40	0.40	0.42	0.27	0.27	0.27	0.27	0.28	0.28	0.19	0.19	0.07
		43	1.63	0.42	0.41	0.41	0.41	0.42	0.28	0.28	0.28	0.28	0.29	0.29	0.18	0.18	0.07
		44	1.64	0.43	0.41	0.41	0.41	0.43	0.28	0.28	0.28	0.28	0.29	0.29	0.18	0.18	0.06
		45	1.65	0.43	0.42	0.42	0.42	0.43	0.28	0.28	0.28	0.28	0.29	0.29	0.18	0.18	0.06
		46	1.66	0.43	0.42	0.42	0.42	0.43	0.29	0.29	0.29	0.29	0.29	0.29	0.17	0.17	0.06
		47	1.67	0.44	0.43	0.43	0.43	0.44	0.29	0.29	0.29	0.29	0.29	0.29	0.17	0.17	0.06
		48	1.68	0.44	0.43	0.43	0.43	0.44	0.29	0.29	0.29	0.29	0.30	0.30	0.17	0.17	0.05
		49	1.69	0.45	0.43	0.43	0.43	0.45	0.30	0.30	0.30	0.30	0.30	0.30	0.16	0.16	0.05
		50	1.70	0.45	0.45	0.45	0.45	0.45	0.30	0.30	0.30	0.30	0.30	0.30	0.16	0.16	0.05
- Ephedrine																	
low	<16mg/ml	5	0.70														
		10	1.00	0.05	0.05	0.05	0.05	0.05					0.05	0.05	0.05	0.05	-0.05
		15	1.18	0.12	0.12	0.12	0.12	0.12					0.12	0.12	0.12	0.12	-0.12
medium	16-25mg/ml	20	1.30	0.17	0.17	0.17	0.17	0.17	0.05	0.05	0.05	0.05	0.17	0.17	0.17	0.17	-0.17
		25	1.40	0.22	0.22	0.22	0.22	0.22	0.08	0.08	0.08	0.08	0.22	0.22	0.22	0.22	-0.22
high	>25mg/ml	30	1.48	0.25	0.25	0.25	0.25	0.25	0.11	0.11	0.11	0.11	0.25	0.25	0.25	0.25	-0.25
		35	1.54	0.28	0.28	0.28	0.28	0.28	0.13	0.13	0.13	0.13	0.28	0.28	0.28	0.28	-0.28
		40	1.60	0.30	0.30	0.30	0.30	0.30	0.15	0.15	0.15	0.15	0.30	0.30	0.30	0.30	-0.30
- Epinephrine																	
very-low	<1ug/min	0.2	-0.70	0.05			-0.05								0.05		-0.05
		0.4	-0.40	0.10			-0.01								0.10		-0.07
		0.6	-0.22	0.13			0.02								0.13		-0.09
		0.8	-0.10	0.14			0.04								0.14		-0.10
low	1-4ug/min	1	0.00	0.16		0.05	0.05	0.05					0.05	0.05	0.16	0.05	-0.11
		2	0.30	0.22		0.07	0.07	0.10					0.10	0.10	0.19	0.10	-0.13
		3	0.48	0.26		0.09	0.09	0.13					0.13	0.13	0.21	0.13	-0.14
		4	0.60	0.28		0.10	0.10	0.14					0.14	0.14	0.22	0.14	-0.15
medium	5-20ug/min	5	0.70	0.31	0.05	0.10	0.10	0.16	0.05	0.05	0.05	0.05	0.16	0.16	0.23	0.16	-0.16
		6	0.78	0.32	0.06	0.11	0.11	0.19	0.08	0.08	0.08	0.08	0.19	0.19	0.24	0.18	-0.19
		7	0.85	0.34	0.07	0.11	0.11	0.22	0.10	0.10	0.10	0.10	0.22	0.22	0.24	0.19	-0.22
		8	0.90	0.35	0.08	0.12	0.12	0.24	0.12	0.12	0.12	0.12	0.24	0.24	0.25	0.20	-0.24
		9	0.95	0.36	0.09	0.12	0.12	0.27	0.14	0.14	0.14	0.14	0.27	0.27	0.26	0.21	-0.27
		10	1.00	0.37	0.10	0.13	0.13	0.28	0.16	0.16	0.16	0.16	0.28	0.28	0.26	0.22	-0.28
		12	1.08	0.38	0.11	0.13	0.13	0.32	0.19	0.19	0.19	0.19	0.32	0.32	0.27	0.24	-0.32
		14	1.15	0.40	0.12	0.14	0.14	0.35	0.21	0.21	0.21	0.21	0.35	0.35	0.27	0.25	-0.35
		16	1.20	0.41	0.13	0.14	0.14	0.37	0.23	0.23	0.23	0.23	0.37	0.37	0.28	0.26	-0.37
		18	1.26	0.42	0.14	0.15	0.15	0.39	0.25	0.25	0.25	0.25	0.39	0.39	0.29	0.27	-0.39
		20	1.30	0.43	0.15	0.15	0.15	0.41	0.27	0.27	0.27	0.27	0.41	0.41	0.29	0.28	-0.41
high	>20ug/min	21	1.32	0.43	0.18	0.18	0.18	0.42	0.27	0.27	0.27	0.27	0.42	0.42	0.29	0.28	-0.42
		23	1.36	0.44	0.24	0.24	0.24	0.43	0.29	0.29	0.29	0.29	0.43	0.43	0.30	0.29	-0.43
		25	1.40	0.45	0.30	0.30	0.30	0.45	0.30	0.30	0.30	0.30	0.45	0.45	0.30	0.30	-0.45
-EpiCalc																	
very-low	<1ug/min	0.2	-0.70	0.05			-0.05								0.05		-0.05
		0.4	-0.40	0.10			-0.01								0.10		-0.07
		0.6	-0.22	0.13			0.02								0.13		-0.09
		0.8	-0.10	0.14			0.04								0.14		-0.10
low	1-4ug/min	1	0.00	0.16		0.05	0.05	0.05					0.05	0.05	0.16	0.05	-0.11
		2	0.30	0.22		0.07	0.07	0.10					0.10	0.10	0.19	0.10	-0.13
		3	0.48	0.26		0.09	0.09	0.13					0.13	0.13	0.21	0.13	-0.14
		4	0.60	0.28		0.10	0.10	0.14					0.14	0.14	0.22	0.14	-0.15
medium	5-20ug/min	5	0.70	0.31	0.05	0.10	0.10	0.16	0.05	0.05	0.05	0.05	0.16	0.16	0.23	0.16	-0.16
		6	0.78	0.32	0.06	0.11	0.11	0.19	0.08	0.08	0.08	0.08	0.19	0.19	0.24	0.18	-0.19
		7	0.85	0.34	0.07	0.11	0.11	0.22	0.10	0.10	0.10	0.10	0.22	0.22	0.24	0.19	-0.22

THERAPY	DOSAGE	conc	log	HR	ABPS	APM	ABPD	SVRI	PAPS	PAPM	PAPD	PVRI	CVP	WP	CI	SI	URINE
		8	0.90	0.35	0.08	0.12	0.12	0.24	0.12	0.12	0.12	0.12	0.24	0.24	0.25	0.20	-0.24
		9	0.95	0.36	0.09	0.12	0.12	0.27	0.14	0.14	0.14	0.14	0.27	0.27	0.26	0.21	-0.27
		10	1.00	0.37	0.10	0.13	0.13	0.28	0.16	0.16	0.16	0.16	0.28	0.28	0.26	0.22	-0.28
		12	1.08	0.38	0.11	0.13	0.13	0.32	0.19	0.19	0.19	0.19	0.32	0.32	0.27	0.24	-0.32
		14	1.15	0.40	0.12	0.14	0.14	0.35	0.21	0.21	0.21	0.21	0.35	0.35	0.27	0.25	-0.35
		16	1.20	0.41	0.13	0.14	0.14	0.37	0.23	0.23	0.23	0.23	0.37	0.37	0.28	0.26	-0.37
		18	1.26	0.42	0.14	0.15	0.15	0.39	0.25	0.25	0.25	0.25	0.39	0.39	0.29	0.27	-0.39
		20	1.30	0.43	0.15	0.15	0.15	0.41	0.27	0.27	0.27	0.27	0.41	0.41	0.29	0.28	-0.41
high	>20ug/min	21	1.32	0.43	0.18	0.18	0.18	0.42	0.27	0.27	0.27	0.27	0.42	0.42	0.29	0.28	-0.42
		23	1.36	0.44	0.24	0.24	0.24	0.43	0.29	0.29	0.29	0.29	0.43	0.43	0.30	0.29	-0.43
		25	1.40	0.45	0.30	0.30	0.30	0.45	0.30	0.30	0.30	0.30	0.45	0.45	0.30	0.30	-0.45
- Norepinephrine																	
	ug/min	1	0.00		0.05	0.05	0.05	0.05	0.05	0.05			0.05	0.05			-0.05
		2	0.30		0.11	0.15	0.15	0.11	0.11	0.11			0.18	0.11			-0.11
		3	0.48		0.14	0.20	0.20	0.14	0.14	0.14			0.25	0.14			-0.14
low	0.04-0.08ug/kg/min	4	0.60		0.16	0.24	0.24	0.16	0.16	0.16	0.05	0.05	0.30	0.16			-0.16
		5	0.70		0.24	0.27	0.27	0.24	0.21	0.21	0.12	0.12	0.33	0.21			-0.24
medium	0.09-0.2ug/kg/min	6	0.78	0.05	0.30	0.30	0.30	0.30	0.25	0.25	0.17	0.17	0.35	0.25	-0.05	-0.05	-0.30
		8	0.90	0.13	0.35	0.35	0.35	0.35	0.31	0.31	0.26	0.26	0.38	0.31	0.01	0.01	-0.35
		10	1.00	0.19	0.38	0.38	0.38	0.38	0.36	0.36	0.33	0.33	0.40	0.36	0.06	0.06	-0.38
		12	1.08	0.24	0.41	0.41	0.41	0.41	0.40	0.40	0.38	0.38	0.42	0.40	0.10	0.10	-0.41
high	>0.2ug/kg/min	15	1.18	0.3	0.45	0.45	0.45	0.45	0.45	0.45	0.45	0.45	0.45	0.45	0.15	0.15	-0.45
Phos.inhibitor																	
- Amrinone																	
low	<5ug/kg/min	0.05	-1.30					-0.05				-0.05			0.05	0.05	
		2	0.30					-0.13				-0.13			0.13	0.13	
		3	0.48					-0.14				-0.14			0.14	0.14	
		4	0.60					-0.15				-0.15			0.15	0.15	
medium	5-15ug/kg/min	5	0.70	0.05	-0.05	-0.05	-0.05	-0.15	-0.05	-0.05	-0.05	-0.15	-0.05	-0.05	0.15	0.15	0.15
		6	0.78	0.09	-0.09	-0.09	-0.09	-0.17	-0.09	-0.09	-0.09	-0.17	-0.06	-0.09	0.17	0.17	0.15
		7	0.85	0.12	-0.12	-0.12	-0.12	-0.19	-0.12	-0.12	-0.12	-0.19	-0.08	-0.12	0.19	0.19	0.15
		8	0.90	0.14	-0.14	-0.14	-0.14	-0.21	-0.14	-0.14	-0.14	-0.21	-0.09	-0.14	0.21	0.21	0.15
		9	0.95	0.16	-0.16	-0.16	-0.16	-0.22	-0.16	-0.16	-0.16	-0.22	-0.10	-0.16	0.22	0.22	0.15
		10	1.00	0.19	-0.19	-0.19	-0.19	-0.23	-0.19	-0.19	-0.19	-0.23	-0.10	-0.19	0.23	0.23	0.15
		12	1.08	0.22	-0.22	-0.22	-0.22	-0.25	-0.22	-0.22	-0.22	-0.25	-0.12	-0.22	0.25	0.25	0.15
		14	1.15	0.25	-0.25	-0.25	-0.25	-0.27	-0.25	-0.25	-0.25	-0.27	-0.13	-0.25	0.27	0.27	0.15
high	>15ug/kg/min	16	1.20	0.28	-0.28	-0.28	-0.28	-0.29	-0.28	-0.28	-0.28	-0.29	-0.14	-0.28	0.29	0.29	0.15
		18	1.26	0.30	-0.30	-0.30	-0.30	-0.30	-0.30	-0.30	-0.30	-0.30	-0.15	-0.30	0.30	0.30	0.15
- Digoxin																	
low	<0.2mg/day	0.1	-1.00	-0.05											0.05	0.05	
medium	2-4mg/day	0.2	-0.70	-0.18											0.08	0.18	
		0.3	-0.52	-0.25											0.10	0.25	
high	>4mg/day	0.4	-0.40	-0.30											0.11	0.30	
		0.6	-0.22	-0.37											0.13	0.37	
		0.8	-0.10	-0.41											0.14	0.41	
		1	0.00	-0.45											0.15	0.45	
CHRONOTROPE																	
Anagonist																	
- Verapamil																	
low	0.05ug/kg or 3mg	1	0.00	-0.05	-0.05	-0.05	-0.05		-0.05	-0.05	-0.05			-0.05	-0.05	-0.05	
		2	0.30	-0.09	-0.09	-0.09	-0.09		-0.09	-0.09	-0.09			-0.09	-0.09	-0.09	
		4	0.60	-0.13	-0.13	-0.13	-0.13		-0.13	-0.13	-0.13			-0.13	-0.13	-0.13	
medium	0.1ug/kg or 7mg	6	0.78	-0.15	-0.15	-0.15	-0.15		-0.15	-0.15	-0.15			-0.15	-0.15	-0.15	
		8	0.90	-0.20	-0.20	-0.20	-0.20		-0.20	-0.20	-0.20			-0.20	-0.20	-0.20	
		10	1.00	-0.23	-0.23	-0.23	-0.23		-0.23	-0.23	-0.23			-0.23	-0.23	-0.23	
high		15	1.18	-0.30	-0.30	-0.30	-0.30		-0.30	-0.30	-0.30			-0.30	-0.30	-0.30	
- Edrophonium																	
	mg	1	0.00	-0.05											-0.05	-0.05	
		5	0.70	-0.29											-0.11	-0.11	
		10	1.00	-0.39											-0.14	-0.14	
		12	1.08	-0.42											-0.14	-0.14	
		15	1.18	-0.45											-0.15	-0.15	
- Atropine																	
	mg	0.50	-0.30	0.05	0.05	0.05	0.05						-0.05	-0.05	0.05	0.05	
	20ug/kg	1.00	0.00	0.20	0.09	0.09	0.09						-0.09	-0.09	0.09	0.09	
		1.50	0.18	0.30	0.11	0.11	0.11		-0.05	-0.05	-0.05		-0.11	-0.11	0.11	0.11	
	40ug/kg	2.00	0.30	0.36	0.13	0.13	0.13		-0.09	-0.09	-0.09		-0.13	-0.13	0.13	0.13	
		3.00	0.48	0.45	0.15	0.15	0.15		-0.15	-0.15	-0.15		-0.15	-0.15	0.15	0.15	
- Propranolol																	
	mg	0.50	-0.30	-0.05	-0.05	-0.05	-0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	-0.05	-0.05	
		1.00	0.00	-0.13	-0.08	-0.08	-0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08	-0.08	-0.08	
		2.00	0.30	-0.22	-0.12	-0.12	-0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12	-0.12	-0.12	
		3.00	0.48	-0.27	-0.14	-0.14	-0.14	0.14	0.14	0.14	0.14	0.14	0.14	0.14	-0.14	-0.14	
		4.00	0.60	-0.30	-0.15	-0.15	-0.15	0.15	0.15	0.15	0.15	0.15	0.15	0.15	-0.15	-0.15	
- Labetalol																	
low	mg/min	1	0.00	-0.05				-0.05							-0.05	-0.05	

THERAPY	DOSAGE	conc	log	HR	ABPS	APM	ABPD	SVRI	PAPS	PAPM	PAPD	PVRI	CVP	WP	CI	SI	URINE
		2	0.30	-0.17				-0.13							-0.13	-0.13	
medium		4	0.60	-0.29	-0.05	-0.05	-0.05	-0.20	-0.05	-0.05	-0.05	-0.05			-0.20	-0.20	
		6	0.78	-0.36	-0.16	-0.16	-0.16	-0.24	-0.09	-0.09	-0.09	-0.09	-0.05	-0.05	-0.24	-0.24	
high		8	0.90	-0.41	-0.24	-0.24	-0.24	-0.28	-0.13	-0.13	-0.13	-0.13	-0.11	-0.11	-0.28	-0.28	
		10	1.00	-0.45	-0.30	-0.30	-0.30	-0.30	-0.15	-0.15	-0.15	-0.15	-0.15	-0.15	-0.30	-0.30	
VASOTROPE																	
- Niprkle																	
low	<1ug/kg/min	0.2	-0.70	0.00	-0.05	-0.05	-0.05	-0.05	0.00	-0.05	-0.05	0.00	-0.05	-0.05	0.05	0.05	0.00
		0.4	-0.40	0.02	-0.10	-0.10	-0.10	-0.10	-0.02	-0.07	-0.07	-0.02	-0.10	-0.10	0.10	0.10	0.00
		0.6	-0.22	0.03	-0.13	-0.13	-0.13	-0.13	-0.03	-0.08	-0.08	-0.03	-0.13	-0.13	0.13	0.13	0.00
		0.8	-0.10	0.04	-0.14	-0.14	-0.14	-0.14	-0.04	-0.09	-0.09	-0.04	-0.14	-0.14	0.15	0.15	0.00
medium	1-4ug/kg/min	1	0.00	0.05	-0.16	-0.16	-0.16	-0.16	-0.05	-0.10	-0.10	-0.05	-0.16	-0.16	0.17	0.17	0.00
		1.2	0.08	0.06	-0.19	-0.19	-0.19	-0.19	-0.06	-0.10	-0.10	-0.06	-0.17	-0.19	0.18	0.18	0.00
		1.4	0.15	0.07	-0.21	-0.21	-0.21	-0.21	-0.07	-0.11	-0.11	-0.07	-0.19	-0.21	0.19	0.19	0.00
		1.6	0.20	0.08	-0.24	-0.24	-0.24	-0.24	-0.08	-0.11	-0.11	-0.08	-0.20	-0.24	0.20	0.20	0.00
		1.8	0.26	0.08	-0.26	-0.26	-0.26	-0.26	-0.08	-0.11	-0.11	-0.08	-0.21	-0.26	0.21	0.21	0.00
		2	0.30	0.09	-0.27	-0.27	-0.27	-0.27	-0.09	-0.12	-0.12	-0.09	-0.21	-0.27	0.22	0.22	0.00
		2.2	0.34	0.09	-0.29	-0.29	-0.29	-0.29	-0.09	-0.12	-0.12	-0.09	-0.22	-0.29	0.23	0.23	0.00
		2.4	0.38	0.10	-0.30	-0.30	-0.30	-0.30	-0.10	-0.12	-0.12	-0.10	-0.23	-0.30	0.23	0.23	0.00
		2.6	0.41	0.10	-0.31	-0.31	-0.31	-0.31	-0.10	-0.13	-0.13	-0.10	-0.23	-0.31	0.24	0.24	0.00
		2.8	0.45	0.11	-0.33	-0.33	-0.33	-0.33	-0.11	-0.13	-0.13	-0.11	-0.24	-0.33	0.24	0.24	0.00
		3	0.48	0.11	-0.34	-0.34	-0.34	-0.34	-0.11	-0.13	-0.13	-0.11	-0.25	-0.34	0.25	0.25	0.00
		3.2	0.51	0.11	-0.35	-0.35	-0.35	-0.35	-0.11	-0.13	-0.13	-0.11	-0.25	-0.35	0.25	0.25	0.00
		3.4	0.53	0.12	-0.36	-0.36	-0.36	-0.36	-0.12	-0.13	-0.13	-0.12	-0.26	-0.36	0.26	0.26	0.00
		3.6	0.56	0.12	-0.37	-0.37	-0.37	-0.37	-0.12	-0.13	-0.13	-0.12	-0.26	-0.37	0.26	0.26	0.00
		3.8	0.58	0.12	-0.38	-0.38	-0.38	-0.38	-0.12	-0.14	-0.14	-0.12	-0.26	-0.38	0.27	0.27	0.00
		4	0.60	0.13	-0.38	-0.38	-0.38	-0.38	-0.13	-0.14	-0.14	-0.13	-0.27	-0.38	0.27	0.27	0.00
high	>4ug/kg/min	5	0.70	0.14	-0.42	-0.42	-0.42	-0.42	-0.14	-0.14	-0.14	-0.14	-0.29	-0.42	0.29	0.29	0.00
		6	0.78	0.15	-0.45	-0.45	-0.45	-0.45	-0.15	-0.15	-0.15	-0.15	-0.30	-0.45	0.30	0.30	0.00
- Nitroglycerine																	
low	<1ug/kg/min	0.2	-0.70					-0.05					-0.05	-0.05	0.05	0.05	0.00
		0.4	-0.40					-0.10					-0.13	-0.13	0.10	0.10	0.00
		0.6	-0.22					-0.13					-0.18	-0.18	0.13	0.13	0.00
		0.8	-0.10					-0.15					-0.21	-0.21	0.15	0.15	0.00
medium	1-4ug/kg/min	1	0.00	0.00	-0.05	-0.05	-0.05	-0.17	-0.05	-0.05	-0.05	-0.05	-0.16	-0.16	0.16	0.16	0.00
		2	0.30	0.06	-0.15	-0.15	-0.15	-0.22	-0.15	-0.15	-0.15	-0.15	-0.27	-0.27	0.21	0.21	0.00
		3	0.48	0.09	-0.20	-0.20	-0.20	-0.25	-0.20	-0.20	-0.20	-0.20	-0.34	-0.34	0.25	0.25	0.00
		4	0.60	0.12	-0.24	-0.24	-0.24	-0.27	-0.24	-0.24	-0.24	-0.24	-0.38	-0.38	0.27	0.27	0.00
high	>4ug/kg/min	5	0.70	0.13	-0.27	-0.27	-0.27	-0.29	-0.27	-0.27	-0.27	-0.27	-0.42	-0.42	0.29	0.29	0.00
		6	0.78	0.15	-0.30	-0.30	-0.30	-0.30	-0.30	-0.30	-0.30	-0.30	-0.45	-0.45	0.30	0.30	0.00
-Nitropaste	1-4ug	1	0.00	0.00	-0.05	-0.05	-0.05	-0.17	-0.05	-0.05	-0.05	-0.05	-0.16	-0.16	0.16	0.16	0.00
		2	0.30	0.06	-0.15	-0.15	-0.15	-0.22	-0.15	-0.15	-0.15	-0.15	-0.27	-0.27	0.21	0.21	0.00
		3	0.48	0.09	-0.20	-0.20	-0.20	-0.25	-0.20	-0.20	-0.20	-0.20	-0.34	-0.34	0.25	0.25	0.00
		4	0.60	0.12	-0.24	-0.24	-0.24	-0.27	-0.24	-0.24	-0.24	-0.24	-0.38	-0.38	0.27	0.27	0.00
		5	0.70	0.13	-0.27	-0.27	-0.27	-0.29	-0.27	-0.27	-0.27	-0.27	-0.42	-0.42	0.29	0.29	0.00
		6	0.78	0.15	-0.30	-0.30	-0.30	-0.30	-0.30	-0.30	-0.30	-0.30	-0.45	-0.45	0.30	0.30	0.00
- Nifedipine	PO-mg	10	1.00	-0.05	-0.05	-0.05	-0.05		-0.05	-0.05	-0.05			-0.05	-0.05	-0.05	
		20	1.30	-0.11	-0.11	-0.11	-0.11		-0.11	-0.11	-0.11			-0.11	-0.11	-0.11	
		30	1.48	-0.15	-0.15	-0.15	-0.15		-0.15	-0.15	-0.15			-0.15	-0.15	-0.15	
- Phenylephrine																	
low	0.04-0.08ug/kg/min	1	0.00	-0.05	0.05	0.15	0.05	0.15					0.05	0.05	-0.05		
		2	0.30	-0.11	0.15	0.23	0.15	0.23					0.11	0.11	-0.11		
		4	0.60	-0.18	0.25	0.30	0.25	0.30					0.18	0.18	-0.18		
medium	0.09-0.2ug/kg/min	6	0.78	-0.22	0.31	0.35	0.31	0.35	0.05	0.05	0.05	0.05	0.22	0.22	-0.22	-0.05	-0.05
		8	0.90	-0.24	0.36	0.38	0.36	0.38	0.08	0.08	0.08	0.08	0.24	0.24	-0.24	-0.13	-0.13
high	>0.2ug/kg/min	10	1.00	-0.26	0.39	0.41	0.39	0.41	0.11	0.11	0.11	0.11	0.26	0.26	-0.26	-0.19	-0.19
		15	1.18	-0.30	0.45	0.45	0.45	0.45	0.15	0.15	0.15	0.15	0.30	0.30	-0.30	-0.30	-0.30
ECFV																	
- Lasix																	
low	<10mg/ml	5	0.70														0.05
medium	10-20mg/ml	10	1.00	-0.05	0.05	0.05	0.05	0.05					-0.05	-0.05	-0.05	-0.05	0.18
		15	1.18	-0.06	0.06	0.06	0.06	0.06					-0.06	-0.06	-0.06	-0.06	0.26
		20	1.30	-0.07	0.07	0.07	0.07	0.07					-0.07	-0.07	-0.07	-0.07	0.32
high	>20mg/ml	25	1.40	-0.08	0.08	0.08	0.08	0.08					-0.08	-0.08	-0.08	-0.08	0.36
		30	1.48	-0.09	0.09	0.09	0.09	0.09					-0.09	-0.09	-0.09	-0.09	0.39
		40	1.60	-0.10	0.10	0.10	0.10	0.10					-0.10	-0.10	-0.10	-0.10	0.45
- Crystolloids	100 ml	100	2.00	-0.03	0.03	0.03	0.03						0.03	0.03	0.03	0.03	0.03
	200 ml	200	2.30	-0.08	0.08	0.08	0.08						0.08	0.08	0.08	0.08	0.07
	250 ml	250	2.40	-0.10	0.10	0.10	0.10						0.10	0.10	0.10	0.10	0.08
	500 ml	500	2.70	-0.15	0.15	0.15	0.15						0.15	0.15	0.15	0.15	0.11
	750 ml	750	2.88	-0.18	0.18	0.18	0.18						0.18	0.18	0.18	0.18	0.14
	1000 ml	1000	3.00	-0.20	0.20	0.20	0.20						0.20	0.20	0.20	0.20	0.15
- Albumin 5%																	
	100 ml	100	2.00	-0.15	0.15	0.15	0.15						0.15	0.15	0.15	0.15	0.15

THERAPY	DOSAGE	conc	log	HR	ABPS	APM	ABPD	SVRI	PAPS	PAPM	PAPD	PVRI	CVP	WP	CI	SI	URINE
	200 ml	200	2.30	-0.21	0.21	0.21	0.21						0.21	0.21	0.21	0.21	0.21
	250 ml	250	2.40	-0.24	0.24	0.24	0.24						0.24	0.24	0.24	0.24	0.24
	500 ml	500	2.70	-0.30	0.30	0.30	0.30						0.30	0.30	0.30	0.30	0.30
- Albumin 25%																	
	100 ml	100	2.00	-0.20	0.20	0.20	0.20						0.20	0.20	0.20	0.20	0.20
	200 ml	200	2.30	-0.30	0.30	0.30	0.30						0.30	0.30	0.30	0.30	0.30
- Packed Cells																	
	100 ml	100	2.00	-0.10	0.10	0.10	0.10						0.10	0.10	0.10	0.10	0.10
	200 ml	200	2.30	-0.13	0.13	0.13	0.13						0.13	0.13	0.13	0.13	0.13
	300 ml	300	2.48	-0.15	0.15	0.15	0.15						0.15	0.15	0.15	0.15	0.15
	400 ml	400	2.60	-0.17	0.17	0.17	0.17						0.17	0.17	0.17	0.17	0.17
	500 ml	500	2.70	-0.20	0.20	0.20	0.20						0.20	0.20	0.20	0.20	0.20
-FFP																	
	100 ml	100	2.00	-0.10	0.10	0.10	0.10						0.10	0.10	0.10	0.10	0.10
	200 ml	200	2.30	-0.13	0.13	0.13	0.13						0.13	0.13	0.13	0.13	0.13
	300 ml	300	2.48	-0.15	0.15	0.15	0.15						0.15	0.15	0.15	0.15	0.15
	400 ml	400	2.60	-0.17	0.17	0.17	0.17						0.17	0.17	0.17	0.17	0.17
	500 ml	500	2.70	-0.20	0.20	0.20	0.20						0.20	0.20	0.20	0.20	0.20
-Autotransfusion																	
	100 ml	100	2.00	-0.10	0.10	0.10	0.10						0.10	0.10	0.10	0.10	0.10
	200 ml	200	2.30	-0.13	0.13	0.13	0.13						0.13	0.13	0.13	0.13	0.13
	300 ml	300	2.48	-0.15	0.15	0.15	0.15						0.15	0.15	0.15	0.15	0.15
	400 ml	400	2.60	-0.17	0.17	0.17	0.17						0.17	0.17	0.17	0.17	0.17
	500 ml	500	2.70	-0.20	0.20	0.20	0.20						0.20	0.20	0.20	0.20	0.20
- Lower Limb Elevation				-0.10	0.10	0.10	0.10						0.10	0.10	0.10	0.10	0.00
ANTIARRHYTHMICS																	
-Bretylium																	
low	<2mg/ml	1	0.00														
medium	2-5mg/ml	2	0.30	-0.05	-0.05	-0.05	-0.05								0.05	0.05	
		3	0.48	-0.10	-0.10	-0.10	-0.10								0.07	0.08	
		4	0.60	-0.13	-0.13	-0.13	-0.13								0.08	0.10	
		5	0.70	-0.16	-0.16	-0.16	-0.16								0.09	0.12	
high	>5mg/ml	6	0.78	-0.18	-0.18	-0.18	-0.18								0.10	0.13	
		7	0.85	-0.20	-0.20	-0.20	-0.20								0.11	0.14	
		8	0.90	-0.30	-0.30	-0.30	-0.30								0.15	0.20	
-Xylocaine																	
low	<2mg/ml	1	0.00														
medium	2-5mg/ml	2	0.30	-0.05	-0.05	-0.05	-0.05								0.05	0.05	
		3	0.48	-0.10	-0.10	-0.10	-0.10								0.07	0.08	
		4	0.60	-0.13	-0.13	-0.13	-0.13								0.08	0.10	
		5	0.70	-0.16	-0.16	-0.16	-0.16								0.09	0.12	
high	>5mg/ml	6	0.78	-0.18	-0.18	-0.18	-0.18								0.10	0.13	
		7	0.85	-0.20	-0.20	-0.20	-0.20								0.11	0.14	
		8	0.90	-0.30	-0.30	-0.30	-0.30								0.15	0.20	
-Procanamide																	
low	<2mg/ml	1	0.00														
medium	2-5mg/ml	2	0.30		-0.05	-0.05	-0.05	-0.05							0.05	0.05	
		3	0.48		-0.12	-0.12	-0.12	-0.12							0.07	0.08	
		4	0.60	0.05	-0.18	-0.18	-0.18	-0.18							0.08	0.10	
		5	0.70	0.08	-0.22	-0.22	-0.22	-0.22							0.09	0.12	
high	>5mg/ml	6	0.78	0.11	-0.25	-0.25	-0.25	-0.25							0.10	0.13	
		7	0.85	0.13	-0.28	-0.28	-0.28	-0.28							0.11	0.14	
		8	0.90	0.15	-0.30	-0.30	-0.30	-0.30							0.15	0.20	
Miscellaneous Medications																	
- Ativan/LorazepamSL mg		2	0.30	-0.05	-0.05	-0.05	-0.05										
		4	0.60	-0.09	-0.09	-0.09	-0.09										
		6	0.78	-0.12	-0.12	-0.12	-0.12										
		8	0.90	-0.14	-0.14	-0.14	-0.14										
		10	1.00	-0.15	-0.15	-0.15	-0.15										
- Morphine	mg	2	0.30	-0.05	-0.05	-0.05	-0.05										
		4	0.60	-0.09	-0.09	-0.09	-0.09										
		6	0.78	-0.12	-0.12	-0.12	-0.12										
		8	0.90	-0.14	-0.14	-0.14	-0.14										
		10	1.00	-0.15	-0.15	-0.15	-0.15										
- Midazolam	mg/ml	2	0.30	-0.05	-0.05	-0.05	-0.05										
		4	0.60	-0.09	-0.09	-0.09	-0.09										
		6	0.78	-0.12	-0.12	-0.12	-0.12										
		8	0.90	-0.14	-0.14	-0.14	-0.14										
		10	1.00	-0.15	-0.15	-0.15	-0.15										
- Librium	mg	5	0.70	-0.05	-0.05	-0.05	-0.05										
		10	1.00	-0.12	-0.12	-0.12	-0.12										
		20	1.30	-0.19	-0.19	-0.19	-0.19										
		30	1.48	-0.23	-0.23	-0.23	-0.23										
		40	1.60	-0.26	-0.26	-0.26	-0.26										

THERAPY	DOSAGE	conc	log	HR	ABPS	APM	ABPD	SVRI	PAPS	PAPM	PAPD	PVRI	CVP	WP	CI	SI	URINE
		50	1.70	-0.28	-0.28	-0.28	-0.28										
		60	1.78	-0.30	-0.30	-0.30	-0.30										
- Meperidine	mg	25	1.40	-0.05	-0.05	-0.05	-0.05										
		50	1.70	-0.15	-0.15	-0.15	-0.15										
		75	1.88	-0.20	-0.20	-0.20	-0.20										
		100	2.00	-0.24	-0.24	-0.24	-0.24										
		125	2.10	-0.27	-0.27	-0.27	-0.27										
		150	2.18	-0.30	-0.30	-0.30	-0.30										
- Percocet	mg	2	0.30	-0.05	-0.05	-0.05	-0.05										
		4	0.60	-0.09	-0.09	-0.09	-0.09										
		6	0.78	-0.12	-0.12	-0.12	-0.12										
		8	0.90	-0.14	-0.14	-0.14	-0.14										
		10	1.00	-0.15	-0.15	-0.15	-0.15										
Cardiac Drugs																	
- Captopril	mg	6	0.78		-0.05	-0.05	-0.05	-0.05									
		12	1.08	0.05	-0.13	-0.13	-0.13	-0.13	-0.05	-0.05	-0.05	-0.05	-0.05	-0.05	-0.05	-0.05	
		15	1.18	0.07	-0.16	-0.16	-0.16	-0.16	-0.07	-0.07	-0.07	-0.07	-0.07	-0.07	-0.07	-0.07	
		20	1.30	0.09	-0.19	-0.19	-0.19	-0.19	-0.09	-0.09	-0.09	-0.09	-0.09	-0.09	-0.09	-0.09	
		25	1.40	0.10	-0.22	-0.22	-0.22	-0.22	-0.10	-0.10	-0.10	-0.10	-0.10	-0.10	-0.10	-0.10	
		50	1.70	0.15	-0.30	-0.30	-0.30	-0.30	-0.15	-0.15	-0.15	-0.15	-0.15	-0.15	-0.15	-0.15	

APPENDIX G – REVERSE PROTOCOLS

11.1 if agent = packed cells
then

(HCT within last 12 hours < 24) or (HB within last 12 hours < 8)
ICU-admission since surgery > 5 hours

11.2 if agent = packed cells
then

(HCT within last 12 hours < 24) or (HB within last 12 hours < 8)
ICU-admission since surgery <= 5 hours

11.3 if agent = ringers lactate or normal saline
then

(OSM within last 6 hours >= 280) and (OSM within last 6 hours <= 300)
weight-gain < 10% admission-weight
(serum Na within last 6 hours >= 135) and (serum Na within last 6 hours <= 150)
(URINE >= 1 ml/kg/hour) or (URINE < 1 ml/kg/hour)
(I/O-balance < -1 litre) or (I/O-balance >= -1 litre)
condition is not ARDS and COPD
crystalloid-therapy not failed

11.4 if agent = D5W
then

(OSM within last 6 hours > 300) or (OSM within last 6 hours < 300)
weight-gain < 10% admission-weight
serum Na within last 6 hours > 150
condition is not ARDS and COPD
crystalloid-therapy not failed

11.5 if agent = 25% albumin
then

OSM within last 6 hours < 295
serum Na within last 6 hours < 150
condition is not ARDS and COPD
(clinical-findings = edema) or (weight-gain > 10% admission-weight)

11.6 if agent = 5% albumin
then

(OSM within last 6 hours >= 295) and (OSM within last 6 hours < 300)
serum Na within last 6 hours < 150
condition is not ARDS and COPD
(clinical-findings = edema) or (weight-gain > 10% admission-weight)

11.7 if agent = fresh-frozen-plasma
then

condition = active-bleeding
PT-INR > 1.8

11.8 if agent = protamine
then

condition = active-bleeding
PTT > 40

11.9 if agent = platelets
then

condition = active-bleeding
platelets < 40,000

11.10 if agent = fresh-frozen-plasma and vitamin-K1
then

condition = active-bleeding
(diagnosis = liver dysfunction) or (pre-op medication = coumadin)

11.11 if agent = amicar
then

condition = active-bleeding
(diagnosis = fibrinolysis) or (D-dimer > 2) or (euglobin-lysis < 90)
fibrinogen = normal

11.12 if agent = amicar and cryoprecipitate
then

condition = active-bleeding
(diagnosis = fibrinolysis) or (D-dimer > 2) or (euglobin-lysis < 90)
fibrinogen < 1.5

11.13 if agent = crystalloid or colloid
then

condition = hypovolemia or hypotension

11.4 if agent = cryoprecipitate
then

condition = active-bleeding
PT > 1.8 and PTT > 40
and fibrinogen < 1.5

APPENDIX H – TECHNICAL DESCRIPTION OF THE PROTOTYPE

DETAILED TECHNICAL DESCRIPTION OF THE PROTOTYPE

A detailed technical description of the prototype is described in this Appendix. Features covered are: the technology platform; the patient data base; the knowledge base for diagnosis; the knowledge base for therapeutic management; the model base; the control knowledge.

TECHNOLOGY PLATFORM

The technology platform describes the hardware, software and network communication resources used in the study.

Hardware

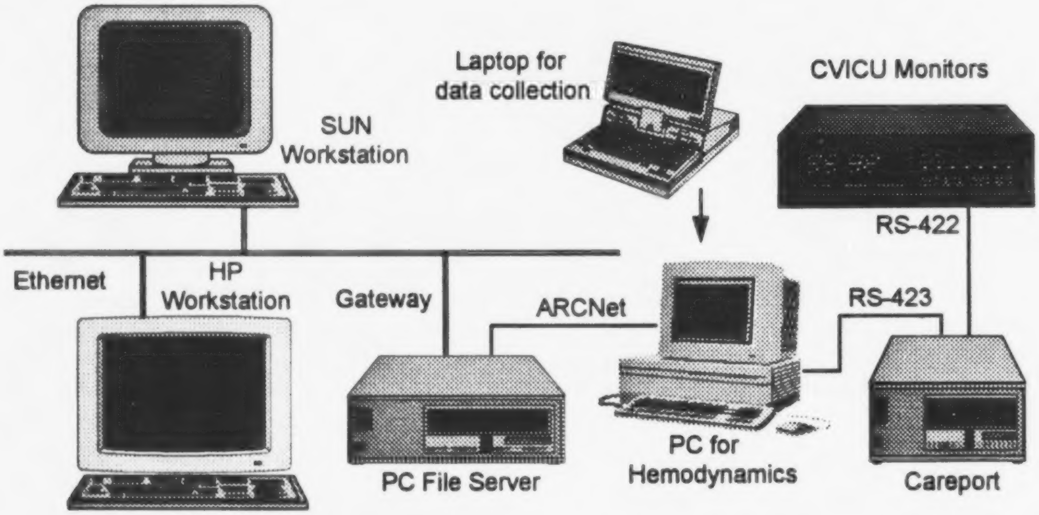
- The prototype was developed on a Unix-based SUN workstation, model ELC-2, with 24 Megabytes (MB) main memory and 400 MB disk storage capacity.
- A Hewlett-Packard Unix-based workstation, model 9000 series 300, with 16 MB main memory and 600 MB disk capacity was used to maintain the patient data files.
- A DOS-based, desktop 80286-PC with 2 MB main memory and 40 MB disk storage was used to collect the patient hemodynamic data from the monitors.
- A laptop 80286-PC with 1 MB main memory and 20 MB disk storage capacity was used by the research nurse to collect the patient's clinical data during the chart review process.
- A DOS-based 80286-PC file server was used as the physical medium to transport the data collected from the monitors on the desktop PC to the Unix machine.

Software

- The commercial Hewlett-Packard (HP) Patient Data Management System (PDMS) model 78592A running on the desktop 80286-PC was used to extract the hemodynamic data from the physiologic monitors in the CVICU.
- Lotus-123 spreadsheet version 3.0 was used to collect the clinical data from the medical charts onto the laptop computer.
- Novell version 2.15 was the network operating system used on the PC file server, where a MICOM TCP/IP gateway software allows the transfer of data to the Unix workstations.
- A PC-based statistical package called Numerical Cruncher Statistical System (NCSS) was used for the analysis of the results.
- The software development environment on the SUN workstation consists of:
  - – Motif X-Window Manager on the SUN Berkerly Unix C-shell operating system
  - – SUN-based C programming language compiler for low-level data manipulation
  - – Commercial expert system shell known as Automated Reasoning Tool for Information Management (ARTIM) from Inference Corporation to develop the prototype

Communications

- The physiologic monitors in the CVICU are connected via a local network that can be accessed using the Careport. The Careport is a communication device used to store hemodynamic data collected from the monitors for up to 24 hours in an electronic buffer.
- The stored hemodynamic data from the buffer can be extracted with the data-save function in the PDMS as ASCII text files onto the desktop PC via a RS-423 serial communication link.
- The SUN workstation is connected to the HP-9000 workstation via a hospital-wide ethernet network, which allowed the HP to be used for storing the patient data files.
- The ethernet allows the hemodynamic data to be transmitted from the PC file server to the HP workstation by using the MICOM TCP/IP communications software package.
- The desktop PC where the PDMS resides is connected to the PC file server via a Novell ARCNet network, which allows data collected from the Careport to be stored on the central file server before being transmitted to the HP.
- The clinical data collected with the Lotus spreadsheet on the laptop PC were first transferred to the desktop PC as exported text files, and then transmitted to the HP via the same route.
- The SUN workstation is connected to the University Computing Science Department via internet that allows routine system backup to be performed on the workstation.
- A configuration of the technical environment is shown below.


Laptop for data collection
CVICU Monitors
SUN Workstation
RS-422
Ethernet
HP Workstation
Gateway
ARCNet
RS-423
PC File Server
PC for Hemodynamics
Careport

PATIENT DATA

There are two categories of patient data. The first includes patient data read from external data files, i.e. hemodynamics, laboratory data and therapeutic interventions. The second are the interpretations, alerts, critiques and recommendations created internally by the system during the reasoning process. Internally, the data are distinguished as: the patient's clinical states; the hemodynamics and their trend; all current and immediate-past laboratory; blood gas and intake-output data; as well as all of the historical data, interpretations, interventions, recommendations and critiques. The different data types are briefly described below.

Patient States

- There are five distinct patient states: previous; current; predicted; proposed; optimal.
- Initially, only the optimal state exists, storing the target ranges pre-defined by the physician. As the patient data are processed, the remaining states would be created and updated over time.
- Each state contains the physiologic patterns for the hemodynamics and trends, laboratory, blood gases, intake-output and coagulation factors, and the clinical conditions identified.
- The states store the patient's physiologic patterns, which are matched to the intervention strategies and condition names (for display purposes).
- Examples of the current and optimal states are shown below. The pattern values and conditions represent the patient state at a given time instant. The optimal state contains the customized target range values for a patient specified by the expert physician.

```
(defschema current-state
        (is-a state)
        (physiology-abg 44044)
        (physiology-coag 44444)
        (physiology-hemo 53020)
        (physiology-hemo-trend 53030)
        (physiology-io 444444)
        (condition (moderate hypovolemia)(mild tachycardia)(moderate hypotension)
                (moderate reduced-filling-pressures)(mildly decreasing-filling-pressure)
                (mildly increasing-heart-rate)(mildly decreasing-mean-arterial-pressure)
                (normal acid-base-balance)(normal io-balance)(normal cogulation)))

(defschema optimal-state
        (APBM  70     85)
        (HR    60     120)
        (CI    2.6    3.4)
        (CVP   10     14)
        (PAPD  10     14))
```

- Intermediate states store the results of the computed difference in hemodynamic values and net-scores between two patient states. The results are used to determine the extent of deviation one state has over another in evaluating the intervention's effectiveness.
- Only a subset of the hemodynamic and intake-output data used for decision-making is included to compute the state difference.
- Six intermediate state schemas are present: predicted-from-optimal-state; predicted-from-proposed-state; proposed-from-optimal-state; current-from-optimal-state; previous-from-optimal-state; current-from-previous-state.
- An example of the current-from-optimal-state is shown below. Each parameter has two values occurring as a sequence (in brackets); the first number is the actual difference, the second being the normalized difference in percent. Parameters with (NIL NIL) have no actual values. NET-DIFF is the net-difference score; the first number is the raw net-score, the second normalized to the number of parameters present (currently just set to the same value as the raw net-score).

```
(DEFSCHEMA CURRENT-FROM-OPTIMAL-STATE
        (ABPD (0 0))
        (ABPM (8 9))
        (ABPS (64 45))
        (CI (NIL NIL))
        (CT (NIL NIL))
        (CT-3HRS (0 0))
        (CVP (NIL NIL))
        (HR (0 0))
        (IO-BALANCE (0 0))
        (NET-DIFF (54 54))
        (PAPD (0 0))
        (PAPM (0 0))
        (PAPD (0 0))
        (PAWP (NIL NIL))
        (PVRI (NIL NIL))
        (SI (NIL NIL))
        (SVRI (NIL NIL))
        (URINE (0 0))
        (URINE-4HRS (0 0))
        (WT (0 0)))
```

Hemodynamics and Trends

- The hemodynamic data read from the external data file are stored in a schema called current-hemodynamics. Interpretation and exponential smoothing are applied to the data and the results are stored in the same schema.

- Each hemodynamic parameter occupies a multi-value slot within the schema, storing for each time point its value, pattern-digit-code, smoothing-average and trend-pattern-digit-code.
- As a new set of hemodynamic data is read, the previous hemodynamic data set is moved to another schema called the previous-hemodynamics for comparison.
- An example of the current-hemodynamics is shown below. Each parameter slot contains a sequence of 7 values: current value; moving average; exponential smoothing average; current pattern digit code; predicted pattern digit code; predicted value based on linear-regression; duration interval for prediction. Moving average, predicted value and duration interval are not used at present.

```
(DEFSCHEMA CURRENT-HEMODYNAMICS
        (IS-A CURRENT-STATE STATE)
        (ABPD (68 AVERAGE 59 4 5 88 DURATION))
        (ABPM (93 AVERAGE 85 5 5 113 DURATION))
        (ABPS (172 AVERAGE 154 6 4 216 DURATION))
        (BSA (NIL AVERAGE SMOOTHED CODE TREND PREDICT DURATION))
        (BTEMP (NIL AVERAGE SMOOTHED CODE TREND PREDICT DURATION))
        (CI (NIL AVERAGE SMOOTHED CODE TREND PREDICT DURATION))
        (CO (NIL AVERAGE SMOOTHED CODE TREND PREDICT DURATION))
        (CONDITION (MILD HYPERTENSION) (NORMAL IO-BALANCE))
        (CVP (NIL AVERAGE SMOOTHED CODE TREND PREDICT DURATION))
        (HR (109 AVERAGE 111 4 4 103 DURATION))
        (HT (NIL AVERAGE 180 CODE TREND PREDICT DURATION))
        (LCW (NIL AVERAGE 5.7 CODE TREND PREDICT DURATION))
        (LCWI (NIL AVERAGE 2.6 CODE TREND PREDICT DURATION))
        (LVSW (NIL AVERAGE 51 CODE TREND PREDICT DURATION))
        (LVSWI (NIL AVERAGE 23.6 CODE TREND PREDICT DURATION))
        (PAPD (12 AVERAGE 13 4 4 12 DURATION))
        (PAPM (17 AVERAGE 17 4 4 18 DURATION))
        (PAPS (22 AVERAGE 22 4 4 23 DURATION))
        (PAWP (NIL AVERAGE SMOOTHED CODE TREND PREDICT DURATION))
        (PULSE (NIL AVERAGE SMOOTHED CODE TREND PREDICT DURATION))
        (PVR (NIL AVERAGE SMOOTHED CODE TREND PREDICT DURATION))
        (PVRI (NIL AVERAGE SMOOTHED CODE TREND PREDICT DURATION))
        (RAP (NIL AVERAGE SMOOTHED CODE TREND PREDICT DURATION))
        (RCW (NIL AVERAGE SMOOTHED CODE TREND PREDICT DURATION))
        (RCWI (NIL AVERAGE 0.63 CODE TREND PREDICT DURATION))
        (RESP (NIL AVERAGE SMOOTHED CODE TREND PREDICT DURATION))
        (RVSW (NIL AVERAGE SMOOTHED CODE TREND PREDICT DURATION))
        (RVSWI (NIL AVERAGE SMOOTHED CODE TREND PREDICT DURATION))
        (SI (NIL AVERAGE SMOOTHED CODE TREND PREDICT DURATION))
        (SV (NIL AVERAGE SMOOTHED CODE TREND PREDICT DURATION))
        (SVR (NIL AVERAGE SMOOTHED CODE TREND PREDICT DURATION))
        (SVRI (NIL AVERAGE SMOOTHED CODE TREND PREDICT DURATION))
        (TEMP (NIL AVERAGE SMOOTHED CODE TREND PREDICT DURATION))
        (VPB (0 AVERAGE 0 4 7 0 DURATION))
        (WT (NIL AVERAGE SMOOTHED CODE TREND PREDICT DURATION)))
```

Laboratory, Blood Gases, Fluid I/O

- The laboratory and blood gas data are stored in the current-laboratory and current-bloodgas schemas, respectively. After the current time has passed, the laboratory and blood gas results are immediately moved over to the "previous" counterparts for storage and comparison.
- Examples of the previous-laboratory and previous-bloodgas schemas are shown below. Each parameter slot contains a sequence with 3 values: actual value; pattern digit code; predicted value (not used at present).

```
(DEFSCHEMA PREVIOUS-LABORATORY
        (IS-A PREVIOUS-STATE STATE)
        (ABNORMALITY-ABG 43200)
        (ABNORMALITY-COAG 34744)
        (ABNORMALITY-HEMO 45040)
        (ABNORMALITY-HEMO-TREND 45040)
        (ABNORMALITY-IO 444444)
        (ABNORMALITY-LAB 32224)
        (ACT (NIL 0 PREDICT))
        (ALB (30 3 PREDICT))
        (BUN (4.7 4 PREDICT))
        (CA (2.21 4 PREDICT))
        (CL (111 7 PREDICT))
        (CO2 (18.5 2 PREDICT))
        (CREAT (86 2 PREDICT))
        (DIGOX (NIL 0 PREDICT))
        (GLU (7.8 4 PREDICT))
        (HB (9.5 4 PREDICT))
        (HCT (27 3 PREDICT))
        (IONCA (1.19 3 PREDICT))
        (K (3.5 2 PREDICT))
        (MG (0.55 2 PREDICT))
        (NA (141 4 PREDICT))
        (OSM (288 4 PREDICT))
        (PHOS (1.03 4 PREDICT))
        (PLT (138 4 PREDICT))
        (PT (1.9 7 PREDICT))
        (PTT (32.9 4 PREDICT))
        (TPRO (NIL 0 PREDICT))
        (WBC (9.7 4 PREDICT)))

(DEFSCHEMA PREVIOUS-BLOODGASES
        (IS-A PREVIOUS-STATE STATE)
        (BASE (-2 4 PREDICT))
        (H (34 3 PREDICT))
        (HCO3 (NIL 0))
        (PCO2 (29 2 PREDICT))
        (PH (NIL 0))
        (PO2 (111 R PREDICT))
        (SAO2 (98 4 PREDICT)))
```

- Intake-output are recorded on the hour only, and all newly arrived data are interpreted and stored in the patient-io schema.
- The patient's cumulative intake-output balance in terms of total fluid intake, blood products received, urine and CT output, and net IO balance are all computed and recorded in another schema called the patient-cumulative-io.
- The two i/o schemas are used to determine the volume status of the patient and are shown below. Each parameter slot in the patient-io schema contains a sequence of 3 values: actual value; pattern digit code; predicted value (not used at present); in patient-cumulative-io, only the actual value is stored in each slot.

```
(DEFSCHEMA PATIENT-IO
        (CT (3 4 PREDICT))
        (CT-3HRS (3 4 PREDICT))
        (IO-BALANCE (0 4 PREDICT))
        (URINE (11.14649681528662 4 PREDICT))
        (URINE-4HRS (3.715498938428875 4 PREDICT))
        (WT (0 4 PREDICT)))

(DEFSCHEMA PATIENT-CUMULATIVE-IO
        (BALANCE-BLOOD -270)
        (BALANCE-FLUID -30)
        (BALANCE-TOTAL -300)
        (BLOOD-IN 0)
        (BLOOD-OUT 270)
        (CT 270)
        (CURRENT-WEIGHT 94.2)
        (EFFECT-DATE-BAL 04-JUL-91)
        (EFFECT-DATE-IN 04-JUL-91)
        (EFFECT-DATE-OUT 04-JUL-91)
        (EFFECT-SECS-BAL 678661200)
        (EFFECT-SECS-IN 678661380)
        (EFFECT-SECS-OUT 678661200)
        (EFFECT-TIME-BAL 1500)
        (EFFECT-TIME-IN 1503)
        (EFFECT-TIME-OUT 1500)
        (INITIAL-HOUR 1901 2000)
        (INITIAL-WEIGHT 94.2)
        (IV 280)
        (OTHER-IN 40)
        (OTHER-OUT 0)
        (TOTAL-INPUT 320)
        (TOTAL-OUTPUT 620)
        (URINE 350)
        (WT 0))
```

Historical Data

- At the end of each cycle, all previous data are stripped down and moved over to the history schemas; these include hemodynamics, laboratory and blood gas data, intake-output, conditions and interventions. Only the median value and the time period are retained.
- At every 24-hour interval, the patient-cumulative-io schema for keeping track of the intake-output is archived and a new one created for the new 24-hour period.
- Historical data are retained for: trend calculation for the hemodynamics; retrieving the last laboratory results for PT, OSM, Na needed in protocol evaluation.
- Because of memory size limitations, only the most recent two-hours of the hemodynamic data were kept in the history-hemodynamics schema.

Interpretations

- For every physiologic pattern constructed from the patient data, an interpretation is done to match it to one or more known clinical conditions.
- Each known condition matched is stored in a new condition schema with a unique key for subsequent retrieval; this allows the tracking of the patient's conditions over time and matching them to the interventions.
- Due to memory limitations, only those conditions within the last hour were retained.
- An example condition schema is shown below. Three slots contain schema names as pointers: physiology-pattern, condition-name and intervention-schema. The condition may point to a specific intervention-nr, which is uniquely assigned for each intervention. The status slot is initially "active" and updated to "complete" once the pattern is no longer present in the current state. The begin-date-time and end-date-time are also updated when initially created and when the pattern is no longer active, respectively.

```
(DEFSCHEMA CONDITION-EVENT--346
        (INSTANCE-OF CONDITION-EVENT)
        (PHYSIOLOGY-PATTERN PHYSIOLOGY--H-43030)
        (PHYSIOLOGY-TYPE HEMO)
        (BEGIN-DATE-TIME ( 4-JUL-91 1436))
        (COMMENT)
        (CONDITION (MILD HYPOTENSION))
        (CONDITION-NAME MILD-HYPOTENSION)
        (CONDITION-NR 7)
        (ELAPSED-TIME 10)
        (END-DATE-TIME (04-JUL-91 1451))
        (INTERVENTION-NR)
        (INTERVENTION-SCHEMA)
        (PATIENT-ID p10128920)
        (RESOLVED-DATE-TIME (04-JUL-91 1458))
        (STATUS COMPLETED))
```

Interventions

- There are two types of interventions: actual; proposed. Both share the same schema structure.
- For each intervention schema, one or more critiques and comments are included where appropriate through the critiquing step.
- An example of an intervention schema is shown below. The instance-of slot determines whether the intervention is actual or proposed. For proposed, the value is proposed-intervention-event.

```
(DEFSCHEMA INTERVENTION-EVENT--214
        (INSTANCE-OF INTERVENTION-EVENT)
        (PHYSIOLOGY-PATTERN)
        (PHYSIOLOGY-TYPE)
        (AGENT NITROGLYCERINE)
        (ASSESS-CRITIQUE)
        (ASSESS-DATE-TIME ( 4-JUL-91 1410))
        (ASSESS-RECORD)
        (ASSESS-SECS 678658200)
        (COMMENT)
        (CONDITION)
        (CRITIQUE-SCHEMA CRITIQUE-EVENT--227)
        (CTLOG-NR 41120)
        (DOSAGE 1)
        (DOSE-CHANGE)
        (DURATION-DATE-TIME ( 4-JUL-91 1355))
        (DURATION-SECS 678657300)
        (FREQUENCY)
        (INTERPRETATION-NR)
        (INTERVENTION-NAME NITROGLYCERINE)
        (INTERVENTION-NR 3)
        (MAXEFFECT-DATE-TIME ( 4-JUL-91 1357))
        (MAXEFFECT-SECS 678657420)
        (ONSET-DATE-TIME ( 4-JUL-91 1357))
        (ONSET-SECS 678657420)
        (OTHER-CRITIQUE CRITIQUE-EVENT--394)
        (PATIENT-ID p10128924)
        (PRINTED-ALREADY)
        (PRINTED-SUMMARY)
        (RESIDUAL-DATE-TIME)
        (RESIDUAL-SECS)
        (RESOLUTION)
        (REVERSE-CRITIQUE)
        (ROUTE CIV)
        (RX-NR 3)
        (SCHEDULE)
        (START-DATE-TIME (04-JUL-91 1355))
        (START-SECS 678657300)
        (STATUS ACTIVE)
        (STOP-DATE-TIME (05-JUL-91 1300))
        (STOP-SECS 678740400)
        (STRENGTH "ug/min"))
```

Selections

- Selections are schemas used to keep track of all active and inactive agents, tests, conditions and any instituted or proposed changes in the interventions for the patient at a given time. It reduces the need to continually look up every condition and intervention schema.
- Two such schemas are used: patient-selections; proposed-selections. Examples of the two schemas are shown below. The slots added, changed and deleted in both schemas are used during each cycle to determine if there has been any changes in the interventions instituted or proposed. Agents no longer active are moved from the active-agent slot to the inactive-agent slot at the end of each cycle. All agents pending become active if the date/time match the current date/time.

```
(DEFSCHEMA PATIENT-SELECTIONS
        (ACTIVE-AGENT (INTERVENTION-EVENT--213 DOPAMINE 8.5 "ug/kg/min")
                        (INTERVENTION-EVENT--214 NITROGLYCERINE 1 "ug/min")
        (ACTIVE-CONDITION CONDITION-EVENT--408 CONDITION-EVENT--429)
        (ADDED (INTERVENTION-EVENT--235 NIPRIDE 0 5))
        (CHANGED)
        (DELETED (INTERVENTION-EVENT--228 KCL 30 0)
                        (INTERVENTION-EVENT--229 CACL2 1000 0))
        (HISTORY-AGENT (INTERVENTION-EVENT--212 EPINEPHRINE 2 "ug/min")
                        (INTERVENTION-EVENT--215 AMICAR 5 MG)
                        (INTERVENTION-EVENT--216 PROTAMINE 50 "mg")
        (INACTIVE-AGENT (INTERVENTION-EVENT--212 EPINEPHRINE 2 "ug/min")
                        (INTERVENTION-EVENT--215 AMICAR 5 MG)
                        (INTERVENTION-EVENT--216 PROTAMINE 50 "mg")
        (PENDING-AGENT (INTERVENTION-EVENT--215 AMICAR 5 MG)
                        (INTERVENTION-EVENT--217 BICARBONATE 50 "mEq")))

(DEFSCHEMA PROPOSED-SELECTIONS
        (ADDED-AGENT)
        (ADDED-TEST)
        (ALTERNATE-AGENT-ACTIVE (ALTERNATE-INTERVENTION--454 NIPRIDE
                                0.6 "ug/kg/min"))
        (ALTERNATE-TEST-ACTIVE)
        (CHANGED-AGENT)
        (CHANGED-TEST)
        (DELETED-AGENT)
        (DELETED-TEST)
        (NEW-INTERVENTION SELECT-COLLOID-CRYSTALLOID-NOW)
        (PROPOSED-AGENT-ACTIVE (ALTERNATE-INTERVENTION--454 NIPRIDE
                                0.6 "ug/kg/min"))
        (PROPOSED-AGENT-INACTIVE)
        (PROPOSED-TEST-ACTIVE (PROPOSED-INTERVENTION--432
                CHECK-HYPERTENSION-IN-10-MINUTES 10 MINUTES))
        (PROPOSED-TEST-INACTIVE (PROPOSED-INTERVENTION--223
                CHECK-CARDIAC-DYSFUNCTION-IN-10-MINUTES 10 MINUTES)
                (PROPOSED-INTERVENTION--225 CONFIRM-LINES-IN-5-MINUTES
                                5 MINUTES)))
```

Critiques

- All recommendations and critiques generated are stored as critique schemas for subsequent display purposes.
- The critiques include proposed diagnostic tests; therapeutic agents; expected magnitude of change in net-score; appropriateness of a therapy instituted.
- For critiques specific to a given intervention, the name of the intervention schema is included; other critiques are identified only by the date and time stamp to indicate the period to which the critique have applied.
- An example of the critique schema is shown below.

```
(DEFSCHEMA CRITIQUE-EVENT--394
        (INSTANCE-OF PROPOSE-CRITIQUE-EVENT)
        (ALTERNATE-SCHEMA ALTERNATE-INTERVENTION--392)
        (CRITIQUE (NITROGLYCERINE @ 0.2 "ug/min" PROPOSED INSTEAD))
        (CRITIQUE-DATE-TIME (04-JUL-91 1451))
        (CRITIQUE-NR 9)
        (CRITIQUE-SECS 678660660)
        (PRINTED-ALREADY YES)
        (REVERSE-CRITIQUE)
        (XREF-SCHEMA INTERVENTION-EVENT--214))
```

KNOWLEDGE BASE FOR DIAGNOSIS

The knowledge base for diagnosing the patient's condition when given a set of clinical data consists of the physiology patterns, the corresponding conditions, the therapeutic target and standard reference ranges for the parameters, and diagnostic tests; these are discussed below.

Physiologic Patterns

- Six types of physiologic patterns are present: hemodynamic status; hemodynamic trend; blood gases; laboratory; fluid intake-output; coagulation.
- The hemodynamic and trend patterns are constructed from HR, MAP, CI, PAD and CVP; the first pattern as static high/low codes, the second as the direction and magnitude of change.
- The blood gas pattern is constructed from H, pO2 and pCO2 only, with two trailing positions for future expansion.
- The laboratory pattern is constructed from Ion-Ca, K, Mg, CO2 and Ca.
- The intake-output pattern is constructed from Urine, Urine-3HRS, CT, CT-3HRS, IO-Balance and %WT-change.
- The coagulation pattern is constructed from HCT, HB, PT, PTT and PLT.

- Some related patterns, such as the hemodynamic and hemodynamic trend patterns, are grouped in pairs to form group-patterns.
- Most of the patterns are sufficiently specific such that one or more intervention strategies can be assigned directly. If not, the patterns are not assigned any intervention strategies.
- Examples of the physiology patterns are shown below.

```
(defschema physiology-H-53020
        (is-a physiology)
        (physiology-hemo 53020)
        (physiology-type hemo)
        (created 01-APR-92 1600)
        (diff-diagnosis confirm-lines-in-5-minutes)
        (diff-diagnosis trendelenburg-position-in-5-minutes)
        (intervention reduce-volume-deficit-in-5-minutes))

(defschema physiology-HT-53020-43040
        (is-a physiology)
        (physiology-hemo 53020)
        (physiology-hemo-trend 43040)
        (created 01-APR-92 1600)
        (diff-diagnosis confirm-lines-in-5-minutes)
        (diff-diagnosis trendelenburg-position-in-5-minutes)
        (intervention reduce-volume-deficit-in-5-minutes))

(defschema physiology-L-32343
        (is-a physiology)
        (physiology-lab 32343)
        (physiology-type lab)
        (created 01-APR-92 1600)
        (intervention give-potassium)
        (intervention give-calcium)
        (intervention give-magnesium))

(defschema physiology-CI-33454-443444
        (is-a physiology)
        (physiology-coag 33454)
        (physiology-io 443444)
        (created 01-APR-92 1600)
        (diff-diagnosis)
        (intervention treat-coagulopathy-now)
        (intervention stop-active-bleeding-now))
```

Clinical Conditions

- Each clinical condition represents a specific problem, along with its degree of severity.
- The conditions were all compiled with the physiology patterns from the learning cases; they include the patient's hemodynamic status, the ionic state, fluid intake-output balance and acid-base status.

- Examples of these conditions are shown below. Each condition can be matched to one or more physiology patterns.

```
(defschema markedly-decreasing-filling-pressures
        (is-a clinical-condition)
        (physiology-hemo-trend 43001 44001 44010 45010 44470 54470)
        (severity markedly)
        (condition decreasing-filling-pressures))

(defschema mild-tachycardia
        (is-a clinical-condition)
        (physiology-lab 51030 41041 41045 53204 53344 53404 53244 54030 56044)
        (severity mild)
        (condition tachycardia))

(defschema mild-hypokalemia
        (is-a clinical-condition)
        (physiology-lab 03040 03041 03045 03204 03344 03404 33244 43030 43044)
        (severity mild)
        (condition hypokalemia))

(defschema moderate-hypotension
        (is-a clinical-condition)
        (physiology-hemo 42040 42034 42043 41001 41002 41003 41004 41005 62010)
        (severity moderate)
        (condition hypotension))
```

Reference Ranges

- All of the physiologic parameters have been assigned reference ranges for classification. Each range gives the physiologic limits, critical, alert and warning levels, both high and low thresholds. The thresholds are used for input data validation and the generation of a pattern-digit-code between 0-7 for the given parameter.
- Examples of the physiologic parameters with their reference ranges are shown below.

```
                              ranges: low -limit -crit -alert -warn -warn -alert -crit -limit high
(defschema reference-ranges
        (APBM  (mean-arterial-pressure          30 50 60 70 85 100 110 120))
        (HCT   (hematocrit                      10 24 26 28 48 50 52 60))
        (HR    (heart-rate                      30 40 50 60 120 130 140 160))
        (CI    (cardiac-index                   2.0 2.2 2.4 2.6 3.5 4.0 4.5 5.0))
        (CVP   (central-venous-pressure                 -10 4 8 10 14 16 18 30))
        (K     (potassium                       2.5 3.5 4.0 5.0 5.2 5.5 5.8 7.0))
        (SVRI  (systemic-vascular-resist-index  1000 1400 1700 2000 2400 2800 3150))
        (URINE (urine-output-per-kg             0 0 0.3 0.4 30.0 60.0 90.0 100.0))
        (WT    (weight-gain-loss-percentage     -50 -20 -10 0 10 20 30 50)))
```

Diagnostic Strategies

- Diagnostic tests are used to confirm or rule out the presence of certain clinical conditions and to check for obstruction or re-zeroing of the catheter lines.
- Each test has a "wait-interval" that specifies the time duration that must elapse before the test can be invoked. When the test is invoked, the corresponding message is displayed, signalling the need to perform the test accordingly.
- Examples of these diagnostic strategies are shown below.

```
(defschema trendelenburg-position-in-10-minutes
        (is-a diagnostic-procedure)
        (ctlog-nr 710000001)
        (look-back (1 hours))
        (message "put in Trendelenburg-position for change in ABP/CVP")
        (procedure-group trendelenburg-position)
        (test-duration (0 minutes))
        (wait-interval (10 minutes))

(defschema check-lines-in-5-minutes
        (is-a diagnostic-procedure)
        (ctlog-nr 710000005)
        (look-back (1 hours))
        (message "No data from CVP/ART lines, confirm for unavailability")
        (procedure-group check-lines)
        (test-duration (0 minutes))
        (wait-interval (5 minutes))
```

KNOWLEDGE BASE FOR THERAPEUTIC MANAGEMENT

Several types of knowledge on drugs and dosage responses are required to generate therapeutic management recommendations: therapeutic agents; drug-dosage responses; therapeutic strategies; therapeutic protocols; criteria for redefining hemodynamic parameter ranges and weaning of drugs. These knowledge types are described below.

Therapeutic Agents

- Each therapeutic agent has been set up as a schema and contains certain pharmacologic knowledge.
- For simplicity, all of the drugs including colloids, crystalloids, inotropes and vasodilators are assumed to be able to reach maximal effect within 15 minutes and would always be assessed for their effectiveness at the end of the 15-minute period.

- An example of a therapeutic agent is shown below.

```
(defschema nitroglycerine
        (is-a therapeutic-agent)
        (assess (15 30 60 minutes))
        (class colloid)
        (ctlog-nr 41120)
        (dose-response-model log)
        (effect-duration (1 2 4 hours))
        (infusion-interval (0 minutes))
        (look-back (1 hours))
        (onset (5 10 15 minutes))
        (max-effect (5 10 15 minutes))
        (route CIV)
        (strength mg/min)
        (unit-amount 0.05))
```

Drug-Dosage Response Tables

- For therapeutic agents that have a hemodynamic response, the magnitude of the effects are quantified in drug-dosage schemas for the commonly used dosage levels.
- The inclusion of dosage responses for agents such as morphine and percocet is to determine their residual effects on the blood pressures, not for the selection of an alternate drug.
- Examples of the drug-dosage response schems are shown below.

```
(defschema nitroglycerine-0.2
        (is-a nitroglycerine)
        (dosage 0.2)
        (ABPD  0)
        (ABPM  0)
        (ABPS  0)
        (CI    0.05)
        (CVP   -0.05)
        (HR    0)
        (PAPD  0)
        (PAPM  0)
        (PAPS  0)
        (PAWP  -0.05)
        (PVRI  0)
        (SI    0.05)
        (SVRI  -0.05)
        (URINE 0))
```

```
(defschema nitroglycerine-1
        (is-a nitroglycerine)
        (dosage 1)
        (ABPD  -0.05)
        (ABPM  -0.05)
        (ABPS  -0.05)
        (CI    0.16)
        (CVP   -0.16)
        (HR    0)
        (PAPD  -0.05)
        (PAPM  -0.05)
        (PAPS  -0.05)
        (PAWP  -0.16)
        (PVRI  -0.05)
        (SI    0.16)
        (SVRI  -0.17)
        (URINE 0))
```

Intervention Strategies

- Intervention strategies are schemas covering general therapeutic and diagnostic strategies, rather than for a tactic leading to a specific choice of agent or test.
- A distinctive feature with intervention strategies is the built-in time delay before the strategy can be invoked.
- Other interventions that are set up as diagnostic tests at present include checking for hypertension, cardiac-dysfunction and dysrhythmia. They are only "place-holders" awaiting future replacement with the appropriate protocols.
- Examples of the intervention strategies created as schemas in the system are shown below.

```
(defschema reduce-volume-deficit-now
        (is-a intervention-procedure)
        (look-back (1 hours))
        (message)
        (procedure-group reduce-volume-deficit)
        (wait-interval (0 minutes)))

(defschema reduce-volume-deficit-in-5-minutes
        (is-a intervention-procedure)
        (look-back (1 hours))
        (message none)
        (procedure-group reduce-volume-deficit)
        (wait-interval (5 minutes)))

(defschema reduce-volume-deficit-in-10-minutes
        (is-a intervention-procedure)
        (look-back (1 hours))
        (message none)
        (procedure-group reduce-volume-deficit)
        (wait-interval (10 minutes)))

(defschema wean-agent-now
        (is-a intervention-procedure)
        (look-back (1 hours))
        (message "weaning of agent suggested since patient has been stable")
        (procedure-group wean-agent)
        (wait-interval (10 minutes)))

(defschema stop-active-bleeding-now
        (is-a intervention-procedure)
        (look-back (1 hours))
        (message "return to O.R. to stop bleeding if needed")
        (procedure-group stop-bleeding)
        (wait-interval (0 minutes)))
```

Therapeutic Protocols

- The therapeutic protocols for volume resuscitation have been set up as ARTIM rules to be invoked when the corresponding intervention strategies are activated after the pre-defined wait-intervals have elapsed.
- The rules are used to select a specific fluid therapy by determining the ionic state, HCT and HB level of the patient at the time.
- In active bleeding, the rules examine the most recent laboratory results for coagulation factors such as PT, PTT and PLT to determine the type of blood product and/or drug to be used.
- A conditional check has been included such that if the proposed agent has been recommended earlier within a predefined time interval, it would not be repeated again. Rather, a message of "agent already proposed earlier" is displayed.
- Also embedded within each rule is the dosage-response computation to determine the exact amount of fluid to be recommended using the net-scoring algorithm.
- Once the intervention choice is made, a proposed intervention schema and a critique schema are created to store the recommendation for subsequent display purposes.
- Also updated is the proposed selections schema that contains a summary list of all of the active and inactive proposed agents and tests.
- The basic structure of the protocol rules is illustrated on the following page. The example shows the protocol for using ringers lactate.

```
(defrule PROPOSE-Reduce-Volume-Deficit-10-7
        (schema phase-control
                (phase propose.select.choice)
                (subphase reduce-volume-deficit))
        (schema time-control
                (hemodynamic-date-time (?current-date ?current-time))
                (hemodynamic-in-secs ?hemodynamic-secs))
        (schema proposed-selections
                (new-intervention ?schema))
        (schema ?schema
                (is-a intervention-procedure)
                (ctlog-nr ?ctlog-nr)
                (message ?msg)
                (procedure-group reduce-volume-deficit))
        (schema ringers
                (strength ?strength)
                (unit-amount ?unit-amount))
        (schema patient-io
                (WT (?wt ?wt-code ?))
=>      (bind ?osm (last-result lab OSM 6 hours))
        (bind ?na (last-result lab NA 6 hours))
        (if (and (numberp ?osm)(numberp ?na)(number ?wt)(>= ?osm 280)
        (< ?wt 10)(<= ?osm 300)(>= ?na 135)(<= ?na 150)) then
                (bind ?agent ringers)
                (bind ?total-needed (* ?needed ?unit-amount))
                (bind ?schema (already-proposed ?agent))
                (if (/= ?schema NIL) then
                   (bind ?critique (build$ ?agent already proposed earlier))
                   (write-critique-only ?schema ?agent ?needed ?critique))
                else
                   (bind ?agent-seq (load-alternate-proposed-agent ?agent ?total ?strength))
                   (bind ?agent (nth$ ?agent-seq 1))
                   (bind ?needed (nth$ ?agent-seq 2))
                   (bind ?critique (build$ ?agent @ ?needed ?strength or normal saline proposed
                        for normal OSM and Na))
                   (bind ?schema (write-intervention-n-critique ?agent ?needed ?strength))
                   (bind ?seq (build$ ?schema ?agent ?needed ?strength))
                   (put-schema-value proposed-selections proposed-agent-active ?seq)
                   (write-critique-only ?schema packed-cells ?*packed-cells-needed*)
                   (put-schema-value proposed-selections alternate-agent-active ?seq)
                   (update-status-change therapy proposed))))
```

- One rule examines alternative therapy options whenever there is a change in the current therapy. Alternatives can be one of an inotrope, vasoactive agent, colloid or crystalloid. At present, only other dosage levels of the same agent are considered when the current dosage level of the agent is being changed.

```
(defrule PROPOSE-Alternative-Drugs
          (schema phase-control
                    (phase propose.select.drugs)
          (schema time-control
                    (hemodynamic-date-time (?current-date ?current-time))
                    (hemodynamic-in-secs ?current-secs)
                    (admit-in-secs ?admit-secs))
=>        (if (not (slot-null phase-control therapy-changed)) then
             (if (not (slot-null patient-selections added)) then
                (bind ?add-seq (get-schema-value patient-selections added))
                (for ?added in$ ?add-seq do
                    (bind ?agent (nth$ added 2))
                    (bind ?name ?agent))
                    (bind ?intervention (nth$ ?added 1))
                    (bind ?start-secs (get-schema-value ?intervention start-secs))
                    (if (> ?start-secs ?admit-secs) then
                       (bind ?class (get-schema-value ?agent class))
                       (if (member$ ?class ?*classes*) then
                          (if (has-children ?agent) then
                              (bind ?proposed (find-alternate-drug ?added add active ?*classes*))
                              (bind ?proposed-schema (nth$ ?proposed 1))
                              (bind ?agent (nth$ ?proposed 2))
                              (bind ?dosage (nth$ ?proposed 4))
                              (if (eq ?agent ?*nochange*) then
                                 (bind ?critique (build$ no change in ?name proposed instead))
                                 (write-critique-other ?proposed-schema ?intervention ?critique
                                                 ?current-date ?current-time)
                               else
                                 (if (/= ?agent ?*already-proposed*) then
                                    (bind ?strength (get-schema-value ?agent strength))
                                    (if (same-alternative ?proposed ?added) then
                                        (bind ?critique (build$ ?agent therapy is appropriate))
                                     else
                                        (if (eq ?dosage 0) then
                                           (bind ?critique (build$ discontinuation of ?agent proposed))
                                         else
                                           (bind ?critique (build$ ?agent @ ?dosage ?strength
                                                     proposed instead)))
                                  (bind ?critique (build$ ?agent @ ?dosage ?strength proposed))
                                  (write-critique-other ?proposed-schema ?intervention ?critique
                                                 ?current-date ?current-time)
                                  (bind ?seq *build$ ?proposed-schema ?agent ?dosage ?strength)
                                  (put-schema-value proposed-selections proposed-agent-active ?seq)
                                  (update-status-change therapy proposed))))
       ...... change and deletion to continue but not shown
```

- A rule specifically checks for the use of vasodilators; the recommendation is to wean down the vasodilator if feasible. This is first checked by computing the hemodynamic effects and net-scores using the different dosage-response schemas and determining if weaning could lead to a lower net-score. This rule is shown below.

```
(defrule MANAGE-Check-Vasodilator
        (schema phase-control
                (phase manage.check.agent)
                (elapsed-time ?elapsed))
        (schema patient-selections
                (active-agent (?intervention ?agent ?dosage ?unit))
        (schema ?agent
                (class vasodilator))
        (schema current-hemodynamics
                (SVRI (?svri ? ? ?svri-code $?))
                (SVR (?svr ? ? ?svr-code $?))
                (CO (?co ? ? ?co-code $?))
                (CI (?ci ? ? ?ci-code $?))
=>      (bind ?check no)
        (if (and (numberp ?ci-code)(numberp ?svri-code)) then
          (if (and (> ?ci-code ?*low-warning-code*)(<= ?svri-code ?*low-warning-code*)) then
            (bind ?check yes))
         else
          (if (and (numberp ?co-code)(numberp ?svri-code)) then
            (if (and (> ?co-code ?*low-warning-code*)(<= ?svri-code ?*low-warning-code*)) then
              (bind ?check yes))
         else
          (if (and (numberp ?co-code)(numberp ?svr-code)) then
            (if (and (> ?co-code ?*low-warning-code*)(<= ?svr-code ?*low-warning-code*)) then
              (bind ?check yes))
         else
          (if (and (numberp ?ci-code)(numberp ?svr-code)) then
            (if (and (> ?ci-code ?*low-warning-code*)(<= ?svr-code ?*low-warning-code*)) then
              (bind ?check yes))))))
        (if (eq ?check yes) then
          (build-combined-effects initialize)
          (bind ?changed (build$ ?intervention ?agent ?dosage ?dosage))
          (bind ?proposed (find-alternate-drug ?changed change vasodilator ?*vasodilator*))
          (bind ?proposed-schema (nth$ ?proposed 1))
          (bind ?agent (nth$ ?proposed 2))
          (bind ?dosage (nth$ ?proposed 4))
          (if (schemap ?agent) then
            (bind ?route (get-schema-value ?agent route)))
          (if (and (/= ?agent ?*nochange*)(/= ?old-dosage ?dosage))
            (not (same-alternative ?proposed ?changed))
            (not (and (eq ?dosage 0)(eq ?route CIV)))(not-active-proposal ?proposed)) then
            (bind ?strength (get-schema-value ?agent strength))
            (if (> ?dosage 0) then
               (bind ?critique (build$ ?agent @ ?dosage ?strength proposed))
             else
   ...... continuation of the rule not shown
```

Reverse Protocols

- Reverse protocols have been set up as a series of ARTIM rules. Their purpose is to determine the appropriateness of a therapeutic agent that has been instituted by checking to see if all the criteria that warrant the use of that agent have been met.
- At present, the interventions checked are: packed-cells, albumins, ringers, D5W, cryoprecipitate, protamine, diuretics, fresh-frozen-plasma, protamine, amicar, bicarbonate, Mg, K, and Ca.
- The rules are invoked every time there is a change in the active-agents slot within the patient-selections schema.
- The criteria used in the RHS of these rules, such as the CT drainage, PLT, PT and PTT levels, are the same as those used in the LHS as patterns that trigger the fluid therapy protocols.
- An example reverse protocol rule for platelets is shown below.

```
(defrule MANAGE-Check-Platelets
         (schema phase-control
                  (phase manage.check.agent)
                  (therapy-changed ?therapy))
         (schema cryoprecipitate
                  (is-a therapeutic-agent))
         (schema patient-selections
                  (added (?schema platelets ?actual ?actual ?unit))
         (schema measure-units
                  (PLT ?plt-unit))
=>       (bind ?ct (last-io-code CT))
         (bind ?ct-3hrs (last-io-code CT-3HRS))
         (if (and (< ?ct ?*high-warning-code*)(< ?ct-3hrs ?*high-warning-code*)) then
            (bind ?critique (build$ no significant bleeding so platelets questionable))
            (bind ?schema (write-critique ?schema ?critique))
          else
            (if (and (< ?ct ?*high-warning-code*)(not (numberp ?ct-3hrs))) then
               (bind ?critique (build$ no significant bleeding so platelets questionable))
               (bind ?schema (write-critique ?schema ?critique)))
         (if (and (< ?ct ?*high-warning-code*)(< ?ct-3hrs ?*high-warning-code*)) then
            (bind ?plt (last-result lab PLT 12 hours))
            (if (numberp ?plt) then
               (if (> ?plt 40) then
                   (bind ?critique (build$ platelets questionable with count @ ?plt ?plt-unit))
                   (bind ?comment (write-critique ?schema ?critique))
            else
               (bind ?critique (build$ no platelets level within last 12 hours so should confirm))
               (bind ?comment (write-critique ?schema ?critique)))
         (if (not (schemap ?comment)) then
            (write-appropriate-therapy ?schema platelets)))
```

Range Redefinition

- An ARTIM rule has been created to examine the need to redefine therapeutic ranges.
- The rule is based on the heuristic that if any one of the patient's MAP, CVP and PAD values within the last two hours have been outside the predefined target range for 75% of the time or more, then the range of that parameter would be redefined to bring the parameter into range.
- The redefinition is done by:
  - – finding the median value of the parameter over the past two hours
  - – looking up a set of predefined ranges for that parameter
  - – choosing the pair that would place the median value in the centre
  - – taking that pair to become the new range
- For simplicity, the rule is invoked for every set of hemodynamic data processed, and the adjustment is immediate as soon as the out-of-range criteria have been met.
- Details of the range redefinition rule are shown below.

```
(defrule PREPARE-Redefine-Range
          (schema phase-control
                    (interval-avg (?interval ?interval-unit))
                    (elapsed-time ?elapsed))
          (schema time-control
                    (hemodynamic-in-secs ?current-secs)
                    (redefine-range (?redefine ?redefine-unit))
                    (redefine-range-fraction ?fraction)
                    (total-hemodynamics-kept (?kept ?kept-unit))
=>        (bind ?redefine-interval (convert-interval-to sec ?redefine ?redefine-unit))
          (bind ?interval (convert-interval-to sec ?kept ?kept-unit))
          (if (< ?kept-interval ?redefine-interval) then
             (printout "** WARNING, insufficient history for redefine interval ")
             (bind ?redefine-interval ?kept-interval))
          (if (not (slot-null time-control last-redefine-in-secs)) then
             (bind ?last-redefine-secs (get-schema-value time-control last-redefine-in-secs))
             (bind ?elapsed (/ ?last-redefine-secs ?interval))
           else
             (bind ?last-redefine-secs 0)
             (bind ?elapsed 0))
          (bind ?last-redefine-secs (+ ?last-redefine-secs ?redefine-interval))
          (if (< ?last-redefine-secs ?current-secs) then
             (for ?parameter in$ ?*redefine-parameter-list* do
                    (if (not-within-range ?parameter ?fraction ?elapsed) then
                       (redefine-range ?parameter ?elapsed)
                       (modify-schema-value time-control last-redefine-in-secs ?last-redefine-secs))))
```

Weaning Protocol

- Another rule deals with the weaning of therapeutic agents once the weaning criteria have been met.
- If the patient's hemodynamics have been within range for a predefined fraction and time interval, then one may attempt weaning down the dosage of the agent, provided that the resulting net-difference score after the weaning is acceptable.
- The within-range fraction and period have been defined to be 80% and two-hours, respectively.
- The rule is invoked for every set of hemodynamic data processed, and the recommendation to wean the agent is displayed as part of the critique in the output.
- This weaning rule is shown below.

```
(defrule PROPOSE-Wean-Agent-Now
         (schema phase-control
                  (phase propose.select.others)
                  (interval-avg (?interval ?interval-unit))
                  (elapsed-time ?elapsed))
         (schema time-control
                  (hemodynamic-date-time (?current-date ?current-time))
                  (hemodynamic-in-secs ?current-secs)
                  (wean-agent-range (?wean-interval ?wean-unit))
                  (wean-not-advised-between (?no-wean-start ?no-wean-stop))
                  (test (or > ?current-time ?no-wean-start)(< ?current-time ?no-wean-stop)))
         (schema patient-selections
                  (active-agent (?intervention ?agent ?dosage ?unit))
         (schema ?intervention
                  (start-secs ?start-secs))
         (schema ?agent
                  (route CIV))
         (schema wean-agent-now
                  (is-a intervention-procedure)
                  (look-back (?look ?look-unit)))
=>       (bind ?wean-secs (convert-interval-to sec ?wean-interval ?wean-unit))
         (bind ?time-limit (- ?current-secs ?wean-secs))
         (if (< ?start-secs ?time-limit) then
            (bind ?time-interval (ceiling (/ ?time-limit ?*minute-to-secs*)))
            (bind ?time-interval (- ?elapsed ?time-interval))
            (if (< ?time-interval 0) then (bind ?time-interval 0))
            (if (within-range ?*wean-parameters* ?time-interval) then
               (bind ?test wean-agent-now)
               (process-intervention ?test ?current-secs ?wait ?wait-unit ?look ?look-unit
                              ?msg ?wait ?wait-unit))))
```

MODEL BASE

Some knowledge sources are parameter-driven mathematical models requiring computations to be performed to derive the results. Examples are the quantitative models for smoothing average calculation and the patient-specific dose response update model. These are described below.

Quantitative Models

- These are for calculating median, simple linear regression, trend-code and exponential smoothing average of the hemodynamic parameter values.
- The models have been implemented as ARTIM functions that can be called from within any rule. An important feature is that the models are dynamically parameter-driven in terms of their input data and processing criteria.
- An exmaple is the exponential smoothing average (ESA) function, which is invoked from within the INTERPRET-Hemodyanmics rule; the ESA is computed and stored in the current-hemodynamics schema.
- The alpha value used is dependent on the number of previous data points, which is updated every time the function is accessed. If no previous ESA exists, the current value is used as the old smoothing average. The ESA schema and function are shown below.

```
(defschema exp-smooth-average
        (is-s quantitative-model)
        (alpha-max (10 0.3))
        (alpha-4 (5 0.4))(alpha-5 (4 0.5))(alpha-6 (3 0.6))
        (size 0))

(def-art-fun compute-exp-smooth-average
        (?current-schema ?previous-schema ?slot)
;       new-smoothed = (alpha * new-value) + ((1 - alpha) * old-smoothed))
;       if no new-smoothed, use old-smoothed, if no old-smoothed, use current-value, else NIL
        (bind ?value (get-parameter-value ?current-schema ?slot VALUE))
        (if (not (schemap ?prevous-schema)) then
          (change-parameter-value ?current-schema ?slot ?value ?value ?value x x x x)
         else
          (bind ?old-smoothed (get-parameter-value ?previous-schema ?slot SMOOTHED))
          (if (not (numberp ?old-smoothed)) then
            (bind ?new-smoothed ?value)
           else
            (bind ?size (get-schema-value exp-smooth-average size))
            (bind ?alpha (get-alpha-value ?size))
            (bind ?x (* ?alpha ?value))
            (bind ?y (- 1 ?alpha))
            (bind ?z (* ?old-smoothed))
            (bind ?new-smoothed (ceiling (+ ?x ?z)))
        (change-parameter-value ?current-schema ?slot x x ?new-smoothed x x x x))
        (bind ?new-size (+ ?size 1))
        (modify-schema-value exp-smooth-average size ?new-size)
```

Computational Drug-Dosage Model

- The computational drug-dosage model consists of several ARTIM rules and callable functions that retrieve the dosage-level schemas with the appropriate expected effects and provide the computation of the hemodynamic effects.
- The process begins when there is an actual or proposed change to the existing therapy. The first step is to look up the appropriate dosage level schema to be used. If no such dosage schema exists, a schema is dynamically created for that dosage level with the logarithmic values of the wo adjacent dosages through linear interpolation of the expected effects.
- When changes are made to two or more agents simultaneously, such as adding one agent and changing the dosage of another, the expected effects from both dosage level schemas are combined using the min-max heuristic before the computation of the net effects.
- The final step is to calculate the expected effects for each hemodynamic parameter value and store them into either the predicted- or proposed-hemodynamics schema depending the rule that called these functions.
- Agents that were not changed are not included in the combined expected effects, since they are assumed to be at maximal effects already with no further impact anticipated on the existing hemodynamic parameters.
- Exceptions are agents with residual effects and active agents not yet reached their maximal effects, in which cases their effects would be prorated according to the elapsed time interval.
- The schemas for initializing and storing the combined expected effects are shown below.

```
(defschema combined-effects-init          (defschema combined-effects
        (ABPD  0.0)                               (ABPD  -0.05)
        (ABPM  0.0)                               (ABPM  -0.05)
        (ABPS  0.0)                               (ABPS  -0.05)
        (CI    0.0)                               (CI     0.16)
        (CVP   0.0)                               (CVP   -0.16)
        (HR    0.0)                               (HR     0)
        (PAPD  0.0)                               (PAPD  -0.05)
        (PAPM  0.0)                               (PAPM  -0.05)
        (PAPS  0.0)                               (PAPS  -0.05)
        (PAWP  0.0)                               (PAWP  -0.16)
        (PVRI  0.0)                               (PVRI  -0.05)
        (SI    0.0)                               (SI     0.16)
        (SVRI  0.0)                               (SVRI  -0.17)
        (URINE 0))                                (URINE 0))
```

- The ARTIM rule that calls the functions to combine the expected effects from the dosage-level schemas when there is a change in the actual therapy is shown below.

```
(defrule COMPUTE-Combine-Effects
        (schema phase-control
                (phase compute.combined.effects)
                (elapsed-time ?elapsed)
                (therapy-changed ?therapy))
        (schema time-control
                (admit-in-secs ?admit-secs)
                (assess-interval (?interval ?interval-unit))
                (hemodynamic-in-secs ?current-secs))
=>      (if (schemap combined-effects) then (schemad combined-effects))
        (copy-schema combined-effects-init combined-effects)
        (bind ?added (get-schema-value patient-selections added))
        (bind ?changed (get-schema-value patient-selections changed))
        (bind ?deleted (get-schema-value patient-selections deleted))
        (bind ?active (get-schema-value patient-selections active-agent))
        (bind ?residual (get-schema-value patient-selections residual-agent))
        (bind ?interval-secs (convert-interval-to sec ?interval ?interval-unit))
        (bind ?next-interval (+ ?current-secs ?interval-secs))
        (invoke-compute-effects ?added ?next-interval ?admit-secs)
        (invoke-compute-effects ?changed ?next-interval ?admit-secs)
        (invoke-compute-effects ?deleted ?next-interval ?admit-secs)
        (invoke-compute-effects ?active ?next-interval ?admit-secs)
        (invoke-compute-effects ?residual ?next-interval ?admit-secs))

(def-art-fun invoke-compute-effects
        (?sequence ?next-interval ?admit-secs)
        (for ?seq in$ ?sequence do
          (bind ?intervention-schema (nth$ ?seq 1))
          (bind ?start-secs (get-schema-value ?intervention-schema start-secs))
          (bind ?onset-secs (get-schema-value ?intervention-schema onset-secs))
          (bind ?agent (nth$ ?seq 2))
          (bind ?has-children no)
          (if (slot-null ?intervention-schema printed-alrady) then
            (if (and (> ?start-secs ?admit-secs)(<= ?onset-secs ?next-interval)) then
               (for ?schema in-schema-children-of ?agent do
                 (bind ?has-children yes))
               (if (/= ?has-children no) then
                 (compute-effects ?seq ?next-interval))
           else
            (bind ?printed-already (get-schema-value ?intervention-schema printed-already))
            (if (eq ?printed-already yes) then
               (bind ?maxeffect-secs (get-schema-value ?intervention-schema maxeffect-secs))
               (if (< ?next-interval ?maxeffects-secs) then
                 (compute-effects ?seq ?next-interval))))
```

- The functions that combine the dosage level schemas and their expected effects are shown below.

```
(def-art-fun compute-effects (?seq ?interval)
          (bind ?intervention (nth$ ?seq 1))
          (bind ?agent (nth$ ?seq 2))
          (bind ?old-dosage (nth$ ?seq 3))
          (bind ?new-dosage (nth$ ?seq 4))
          (bind ?agent-effects (lookup-agent-effects ?agent ?old-dosage ?new-dosage))
          (for ?slot in-slots-of ?agent-effects do
              (if (and (slotp combined-effects ?slot)(/= ?slot is-a)) then
                (bind ?percent (compute-effects-response ?intervention ?agent-effects ?slot ?interval)
                (bind ?old-percent (nth$ (get-schema-value combined-effects ?slot) 1))
                (bind ?new-percent (load-percent ?old-percent ?percent))
                (modify-schema-value combined-effects ?slot ?new-percent)))
         (bind ?result ?agent-effects))

(def-art-fun load-percent (?old-percent ?percent)
          (if (not (numberp ?old-percent)) then (bind ?old-percent 0))
          (if (and (< ?percent 0)(< ?old-percent 0)) then
;             if both percents decrease the parameter, take the min[-a,-b]
             (if (< ?percent ?old-percent) then
                (bind ?new-percent ?percent)
              else
                (bind ?new-percent ?old-percent)))
          (if (and (eq ?percent 0)(eq ?old-percent 0)) then
;             if both have zero effect, then load 0
             (bind ?new-percent 0)
           else
;            otherwise load the nonzero as the new percent
             (if (eq ?percent 0) then
                (bind ?new-percent ?old-percent)
              else
                ((if (eq ?old-percent 0) then (bind ?new-percent ?percent))
          (if (and (> ?percent 0)(> ?old-percent 0)) then
;             if both percents increase the parameter, take the max[a,b]
             (if (> ?percent ?old-percent) then
                (bind ?new-percent ?percent)
             else
                (bind ?new-percent ?old-percent))
          (if (or (and (> ?percent 0)(< ?old-percent 0))(and (< ?percent 0(< ?old-percent 0))
             (and (< ?percent 0)(> ?old-percent 0))) then
;             if one increases, the other decreases, take the difference
             (bind ?new-percent (+ ?percent ?old-percent)))
          (bind ?result ?new-percent))
```

- The ARTIM rule that computes the predicted hemodynamic effects for the next time period as a result of a change in existing therapy is shown below.

```
(defrule COMPUTE-Predict-Next-State
        (schema phase-control
                (elapsed-time ?elapsed)
                (therapy-change ?therapy))
        (schema time-control
                (admit-in-secs ?admit-secs)
                (assess-interval (?interval ?interval-unit))
                (hemodynamic-in-secs ?current-secs))
=>      (bind ?elapsed (+ ?elapsed ?interval))
        (if (not (schdmap predicted-hemodynamics)) then
          (copy-schema patient-hemodynamics predicted-hemodynamics)
          (copy-schema patient-state predicted-state)
          (modify-schema-value predicted-hemodynamics is-a predicted-state))
        (if (and (slot-null patient-selections added)(slot-null patient-selections changed)) then
          (get-default-predictions current-hemodynamics predicted-hemodynamics ?elapsed)
        else
          (predict-combined-effects current-hemodynamics predicted-hemodynamics
                predicted-state ?elapsed))

(def-art-fun predict-combined-effects (?schema-1 ?schema-2 ?state ?elapsed)
        (modify-schema-value ?schema-2 elapsed-time ?elapsed)
        (for ?slot in-slots-of ?schema-2 do
          (if (not (slotp ?state ?slot)) then
            (bind ?old-value (get-parameter-value ?schema-1 ?slot VALUE))
            (if (slotp combined-effects ?slot) then
                (bind ?coeff (nth$ (get-schema-value combined-effects ?slot) 1))
             else
                (bind ?coeff 0.00))
            (if (not (numberp ?coeff)) then (bind ?coeff 0.00))
            (if (/= ?coeff 0.00)(numberp ?old-value)) then
                (bind ?predict (* ?old-value (+ 1.00 ?coeff)))
                (if (intergerp ?old-value) then (bind ?predict (ceiling ?predict)))
                (create-parameter-vector ?schema-2 ?slot ?predict)
                (assign-predict-hemo ?schema-2 ?slot)
                (assign-range-hemo ?schema-2 ?slot)
            else
                (bind ?predict (get-parameter-value ?schema-1 ?slot SMOOTHED))
                (if (numberp ?predict) then
                  (create-parameter-vector ?schema-2 ?slot ?predict)
                  (assign-predict-hemo ?schema-2 ?slot)
                  (assign-range-hemo ?schema-2 ?slot)
                 else
                  (bind ?predict NIL)
                  (create-parameter-vector ?schema-2 ?slot ?predict)
                  (carryover-into ?schema-2 ?schema-1 ?slot linear-trend-hemo)))))
```

The Net-Difference Scoring Model

- The net-difference score is computed for every therapy change implemented or being considered, applicable over the forthcoming time period.
- The score is computed for the current state with no change, the predicted state for any actual change in therapy, and the proposed state for any alternate therapy choice. Then the states are compared and the one with the least score is chosen, to be recommended if different from actual.
- The net-difference scoring algorithm is made up of several functions, callable from a number of ARTIM rules depending on whether one is dealing with the current state with no change, a change in existing therapy or a proposed alternate choice.
- Examples of the rules that compare the current- and predicted-hemodynamic schemas with the optimal state schema are shown below.

```
(defrule COMPARE-Current-To-Optimal
        (schema phase-control
                (phase compare.current.difference)
                (elapsed-time ?elapsed)
                (therapy-changed ?therapy))
=>      (retact-all-schema-values current-from-optimal-state net-diff)
        (compute-difference-from-optimal current-hemodynamics patient-io
                current-from-optimal-state))

(defrule COMPARE-Predicted-To-Optimal
        (schema phase-control
                (phase compare.current.difference)
                (elapsed-time ?elapsed)
                (therapy-changed ?therapy))
=>      (retact-all-schema-values predicted-from-optimal-state net-diff)
        (compute-difference-from-optimal current-hemodynamics patient-io
                predicted-from-optimal-state))
```

- The compute-difference-from-optimal function that performs the net-difference score calculation is shown below.
- The function is also called by the find-alternate-drug function that is used to select the therapeutic agent of choice.

```
(def-art-fun compute-difference-from-optimal (?schema ?schema-2 ?diff-schema)
        (bind ?pa-parameter (get-schema-value patient-devices pa-parameters))
        (for ?slot in-slots-of ?diff-schema do
          (if (slotp reference-ranges ?slot) then
            (for ?seq in$ (get-schema-value reference-ranges ?slot) do
                (bind ?i 1)
                (for ?range in$ ?seq do
                  (if (eq ?i 2) then (bind ?critical-low ?range))
                  (if (eq ?i 3) then (bind ?alert-low ?range))
                  (if (eq ?i 4) then (bind ?warning-low ?range))
                  (if (eq ?i 5) then (bind ?warning-high ?range))
                  (if (eq ?i 6) then (bind ?alert-high ?range))
                  (if (eq ?i 7) then (bind ?critical-high ?range))
                  (bind ?i (+ ?i 1))))
          (bind ?value (get-parameter-value ?schema ?slot VALUE))
          (if (numerp ?value) then
            (bind ?count (+ ?count 1))
            (if (and (>= ?value ?warning-low)(<= ?value ?warning-high)) then
                (bind ?diff 0)(bind ?diff-percent 0)
            else
                (if (< ?value ?warning-low) then
                  (bind ?diff (- ?value ?warning-low))
                  (if (and (< ?value ?alert-low)(>= ?value ?critical-low)) then
                    (bind ?diff (* ?diff ?*alert-weight*)))
                  (if (< ?value ?critical-low) then
                    (bind ?diff (* ?diff ?*critical-weight*)))
                  (bind ?diff-percent (truncate (/ (* 100 (abs ?diff) ?warning-low)))))
                (if (> ?value ?warning-high) then
                  (bind ?diff (- ?value ?warning-high)
                  (if (and (> ?value ?alert-high)(<= ?value ?critical-high)) then
                    (bind ?diff (* ?diff ?*alert-weight*)))
                  (if (> ?value ?critical-high) then
                    (bind ?diff (* ?diff ?*critical-weight*)))
                  (bind ?diff-percent (truncate (/ (* 100 (abs ?diff) ?warning-high))))
          (bind ?net-diff (+ ?net-diff ?diff-percent))
          (bind ?result (build$ ?diff ?diff-percent))
          (if (> ?net-diff 0) then
            (if (eq ?*normalize* no) then
                (bind ?net-diff-adjusted ?net-diff)
            else
                (if (eq ?cardiac-output yes) then
                  (bind ?net-diff-adjusted (ceiling (/ (* ?net-diff ?*total-pa-parameters*) ?count)))
                else
                  (bind ?net-diff-adjusted ?net-diff)))
          (bind ?result (build$ ?net-diff ?net-diff-adjusted)
          (modify-schema-value ?diff-schema net-diff ?result))
```

The Patient-Specific Drug-Dosage Response Model

- ARTIM rules and functions have been implemented to allow the incremental adjustment of the initial pharmacodynamic expected effects with the actual responses over time.
- To simplify the assessment of actual response to therapeutic agents, all of the agents are assessed once they have been instigated for 15 minutes.
- To prepare for an assessment, whenever an agent with a drug-dose level schema is selected, a dosage-event schema is created, storing the "before" hemodynamic values at the time when the agent is initiated. When 15 minutes has passed, an assessment is carried out by comparing the "after" hemodynamic values at that time with those "before" for the percent difference.
- A simple heuristic is used to combine the new differences with the initial expected effects from the dosage-response tables: the initial expected effect for each parameter is prorated according to the computed actual effect at a given dosage level.
- In the case where multiple assessments have been done on the same agent over time, the new actual expected effects are obtained by averaging all the previous ones. This is expected to smooth out the individual variations that may exist.
- The ARTIM rule that sets up the dosage-event and assessment is shown below.

```
(defrule COMPARE-Therapy-Effects
          (schema phase-control
                    (phase compare.therapy.effects)(therapy-changed ?therapy))
=>        (if (not (slot-null patient-selections added)) then
             (bind ?added-seq (get-schema-value patient-selections added))
             (for ?seq in$ ?added-seq do
                (bind ?intervention-schema (nth$ ?seq 1))
                (bind ?agent (nth$ ?seq 2))
                (if (slot-null ?intervention-schema assess-record) then
                    (if (has-dosage-levels ?agent) then
                       (bind ?old-dosage (nth$ ?seq 3))
                       (bind ?dose-schema (write-dosage-event ?intervention-schema ?agent))
                       (bind ?schema (write-assess-event ?seq added ?old-dosage ?dose-schema))
                       (put-schema-schema-value ?intervention-schema assess-record yes)
                       (write-assess-log ?schema))))
          .... also for changed, deleted but not included here ....
```

- The rule that does the actual drug-dosage assessment is shown below.

```
(defrule COMPARE-Therapy-Effects-Now
        (schema phase-control
                (phase compare.therapy.effects))
        (schema ?schema
                (is-a assess-event)
                (agent ?agent)
                (assess-secs ?assess-secs)
                (dosage-schema ?dosage-schema)
        (schema time-control
                (hemodynamic-in-secs ?current-secs))
        (test (eq ?not-assessed ?*not-assessed*))
        (test (<= ?assess-secs ?current-secs))
=>      (bind ?patient-id (nth$ (get-schema-value current-state patient-id) 1))
        (update-dosage-event ?dosage-schema)
        (bind ?dose-table (update-dosage-tables ?dosage-schema ?agent ?patient-id)
        (bind ?ratio-diff (get-schema-value :dose-table ratio-diff))
        (if (> ?ratio-diff 0) then
           (bind ?percent ?ratio-diff)
           (bind ?change (build$ ?percent change in net-diff observed))
         else
           (bind ?change (build$ 0 change in net-diff observed)))
        (bind ?diff (build$ ?ratio-diff ?ratio-diff))
        (modify-schema-value ?schema status ?*assessed*)))

(def-art-fun update-dosage-tables (?dosage-event ?agent ?patient-id)
        (bind ?schema-s (string-append ?patient-id "–"))
        (bind ?schema-sx (string-append ?schema-s ?agent))
        (if (not (schemap ?schema)) then
           (copy-schema drug-dose-parameters ?schema))
        (for ?slot in-slots-of ?dosage-event do
           (if (and (/= ?slot is-a)(slotp compare-parameters ?slot)) then
              (bind ?new-seq (nth$ (get-schema-value ?dosage-event ?slot) 1))
              (bind ?new (nth$ ?new-seq 3))
              (bind ?ratio-diff 0.0)
              (if (not (slot-null ?schema ?slot)) then
                  (bind ?old (nth$ (get-schema-value ?schema ?slot) 1))
               else
                  (bind ?old 0.0))
              (bind ?seq (build$ ?ratio-diff))
              (modify-schema-value ?schema ?slot ?seq))
        (bind ?new-diff (get-schema-value ?dosage-event ratio-diff))
        (if (not (slot-null ?schema ratio-diff)) then
           (bind ?diff (get-schema-value ?schema ratio-diff))
           (bind ?latest (/ (+ ?new-diff ?diff) 2.0))
         else
           (bind ?latest ?new-diff))
        (put-schema-value ?schema intervention-schema ?dosage-event))
```

CONTROL KNOWLEDGE

The use of control knowledge such as the global control variables, the reasoning loop, pattern formation and condition matching, time and intake-output controls, and reasoning of the patient states over time are discussed below.

Global Variables as Controls

- Many numeric values and logic switches used for computation and/or decision-making within the prototype have been set up as global variables, to allow easy update.
- A global variable is defined for the maximum allowable PAD-PAWP difference.
- A global flag is used to control the updating of the general drug-dose response tables.
- Variables are used for severity weight factors for out-of-range hemodynamic parameters.
- A flag is used to normalize the calculated net-score against the number of parameters present.
- An alternate-agent-class sequence provides the agent classes to be included when looking up to choose an alternate agent. Current default classes include colloids, crystalloids, inotropes and vasoactive agents.
- A maximum dosage variable is used to define the maximum dosage levels to be scanned when considering alternate drugs The default maximum dosage levels is "2" to include only those dosage levels that are twice the current level.

The Reasoning Loop

- The reasoning process is conducted in sequential phases, each consisting of one or more rules and an incremental step toward the final conclusion. The phases are summarized below.
- **INPUT**. This begins the execution of the prototype by initializing the variables and reading in a set of the input data.
- **INTERPRET**. This validates the input data, classifies the patterns, interprets the clinical conditions and creates the appropriate patient-specific knowledge structures for reasoning.
- **MANAGE**. This critiques the actual therapies recorded using the reverse protocols.
- **COMPUTE**. This computes the combined-effects and net-different scores for the current and predicted states given the changes in existing therapies.
- **PROPOSE**. This selects the alternate intervention agents using the net-difference score calculation to become the proposed agents in the proposed state.
- **COMPARE**. This compares the current, predicted and proposed states for the best net-score as the final recommendations.
- **INTERACT**. This provides the output either in detailed, summary assessment form, which could either be displayed on the computer screen or printed into a disk file on the system.
- **PREPARE**. This performs the necessary house-keeping tasks by deleting old interventions and critiques, updating the patient states and preparing for the next set of input data.

- A single rule is used to control the reasoning loop. This rule has a value of -10 in its "salience slot", which only fires after all rules within the same phase have been processed.
- PREPARE-End also has a -10 salience value and is the last rule to fire. Its purpose is to reset the phase slot to its first value, so that the program can start another cycle. Portions of the phase-control schema and the two phase-control rules are shown below.

```
(defschema phase-control
        (phase initialize)
        (subphase)(condition-changed)(elapsed-time 0)
        (interval-avg (5 minutes))(interval-trend (15 minutes))
        (phase-after (initialize input.filename))
        (phase-after (input.filename input))
        (phase-after (input input.data))
        (phase-after (input.data input.data.check))
        (phase-after (input.data.check input.data.hemo))
        (phase-after (input.data.hemo input.data.read))
        (phase-after (input.data.read input.data.lab))
        (phase-after (input.data.lab interpret.interventions))
        (phase-after (interpret.interventions interpret.interventions.after))
        (phase-after (interpret.interventions.after interpret.update.ranges))
        (phase-after (interpret.update.ranges interpret.reference.ranges))
        (phase-after (interpret.reference.ranges interpret.cumulative.input))
        (phase-after (interpret.cumulative.input interpret.cumulative.output))
        (phase-after (interpret.cumulative.output interpret.io))
        (phase-after (interpret.io interpret.derive.pattern))
        (phase-after (interpret.derive.pattern interpret.derive.condition))
        (phase-after (interpret.derive.condition interpret.update.condition))
        (phase-after (interpret.update.condition interpret.derive.trend))
        (phase-after (interpret.derive.trend interpret.update.trend))
        (phase-after (interpret.update.trend interpret.update.interpretation))
        (phase-after (interpret.update.interpretation manage.therapy.changes))
        (phase-after (manage.therapy.changes manage.check.electrolytes))
        (phase-after (manage.check.electrolytes manage.check.agent))
        (phase-after (manage.check.agent manage.check.condition))

(defrule CONTROL-Change-Phases
        (declare (salience -10))
        (schema phase-control
                (phase ?current-phase)(phase-after (?current-phase ?next-phase))
=>      (modify-schema-value phase-control phase ?next-phase))

(defrule PREPARE-End
        (schema phase-control   (phase prepare.end))
=>
        (if (not (slot-null phase-control therapy-changed)) then
           (retract-all-schema-values phase-control therapy-changed))
        (if (schemap predicted-state) then
           (retract-all-schema-values predicted-state condition)))
```

- Certain rules within a phase have the ability to load the subphase-after slot of the phase-control schema with values which could be activated at a later time, causing other rules from a different phase to be fired.
- When the physiology-patterns and the clinical conditions are matched during the INTERPRETATION phase, any diagnostic tests and interventions specified in the known patterns are loaded into the subphase-after slot.
- Subsequently, when the PROPOSE phase is activated, the PROPOSE-Subphases rule would look for the presence of any values within the subphase-after slot of the phase-control schema to invoke, which are all of the proposed diagnostic tests and interventions.
- These values are placed into the subphase slot one at a time, and any rules within the PROPOSE phase matching the current subphase value would fire, invoking a particular intervention choice to be selected.
- The PROPOSE-Subphases rule is shown below.

```
(defrule PROPOSE-Subphases
        (schema phase-control
                (phase propose.select.goals)
                (subphase)
                (subphase-after ?))
=>      (if (not (slot-null phase-control subphase-after)) then
          (bind ?seq (get-schema-value phase-control subphase-after))
          (if (member$ continue-to-monitor ?seq) then
            (if (> (length$ ?seq) 1)) then
              (retract-schema-value phase-control subphase-after continue-to-monitor)
              (bind ?seq (get-schema-value phase-control subphase-after))))
          (bind ?monitor no)
          (for ?active in$ ?seq do
            (if (schemap ?active) then (bind ?is-a (get-schema-value ?active is-a)))
            (if (member$ monitor-procedure ?is-a) then
                (modify-schema-value phase-control subphase ?active)
                (modify-schema-value phase-control phase propose.select.choice)
                (retract-schema-value phase-control subphase-after ?active)
                (bind ?seq (get-schema-value pahse-control subphase-after))
                (bind ?monitor yes)))
          (if (eq ?monitor no) then
            (remove-old-monitor)
            (bind ?subphase (nth$ ?seq 1))
            (modify-schema-value phase-control subphase ?subphase)
            (modify-schema-value phase-control phase propose.select.choice)
            (retract-schema-value phase-control subphase-after ?subphase)
            (bind ?seq (get-schema-value phase-control subphase-after))))
```

- An example rule with subphase is PROPOSE-Select-Interventions, used for invoking proposed intervention strategies such as reduce-volume-deficit, treat-coagulopathy, stop-active-bleeding and check-cardiac-dysfunction.
- The rule has a time delay and activation algorithm that can process any strategy with a wait-interval requirement. For instance, if the intervention strategy is reduce-volume-deficit-in-10-minutes, a proposed intervention schema with a pending status is created, with the appropriate date-and-time stamp as to when it was created.
- Any intervention strategy with a pending status is not considered active, and does not appear as a recommendation. If such a strategy has already been created during some past intervals, the date-and-time stamp of that intervention schema is examined to determine if the designated wait-interval has elapsed. If so, the next subphase is activated with that strategy to allow the agent of choice to be selected and recommended according to the predefined protocols.
- An important role of the PROPOSE-Select-Interventions rule is to reconcile the pending diagnostic test and intervention strategies proposed over time.
- At any point in time during the reasoning process, there may be one or more pending intervention schemas created from the previous cycles. These may be intervention strategies with certain wait-intervals that have not expired, such as a pending reduce-volume-deficit-in-10-minutes intervention strategy that is only 5 minutes into the waiting interval.
- One of the functions of this rule is to find out if there is already a pending intervention schema created for the intervention strategy currently under consideration. If so, then the wait-intervals of the two intervention strategies are compared.
- The one with the shorter wait-interval, if not expired, would be written into the original intervention schema along with the new wait-interval. An example is the situation where one could start with a hemodynamic pattern for mild hypovolemia, which would result in a pending intervention schema of reduce-volume-deficit-in-10-minutes to be created.
- If the condition worsen over the next interval, the intervention schema is updated with the new intervention strategy value, which could be to reduce-volume-deficit-in-5-minutes.
- If the wait-interval for a given intervention strategy is zero, or the waiting period has expired for an intervention strategy with an original positive wait-interval, the procedure-group value of the intervention strategy would be loaded into the subphase slot to become the next subphase to be activated to select the intervention choice.
- This group of rules is primarily concerned with selecting the agent of choice for the given strategy, such as choosing normal saline over albumin based on the serum OSM and Na levels.

- The PROPOSE-Select-Interventions rule is shown below.

```
(defrule PROPOSE-Select-Interventions
         (schema phase-control
                  (phase propose.select.choice)
                  (subphase ?action))
         (test (or (eq ?action reduce-volume-deficit-now)
                  (eq ?action reduce-volume-deficit-in-5-minutes)
                  (eq ?action reduce-volume-deficit-in-10-minutes)
                  (eq ?action treat-coagulopathy-now)
                  (eq ?action treat-coagulopathy-in-5-minutes)
                  (eq ?action treat-coagulopathy-in-10-minutes)
                  (eq ?action stop-active-bleeding-now)
                  (eq ?action check-cardiac-dysfunction))
         (schema time-control (hemodynamic-in-secs ?current-secs))
         (schema ?action
                  (is-a intervention-procedure)
                  (look-back (?look ?look-unit))
                  (procedure-group reduce-volume-deficit | stop-bleeding | treat-coagulopathy)
                  (wait-interval (?wait ?wait-unit)))
=>       (delete-choice ?action)
         (bind ?action-group (get-schema-value ?action procedure-group))
         (bind ?inactives (get-schema-value proposed-selections proposed-agent-inactive))
         (bind ?already-proposed (strategy-already-proposed ?look ?look-unit))
         (if (eq ?already-proposed yes) then (bind ?done yes))
         (if (and (/= ?done yes)(> ?wait 0)) then
            (bind ?actives (get-schema-value proposed-selections proposed-agent-active))
            (for ?active in$ ?actives do
               (bind ?name (nth$ ?active 2))
               (bind ?wait-interval (get-schema-value ?name ?wait-interval))
               (bind ?time (nth$ ?wait-interval 1))
               (bind ?procedure-group (get-schema-value ?name procedure-group))
               (if (or (eq ?action-group ?procedure-group)(eq ?name ?action)) then
                  (bind ?done yes)
                  (bind ?stop-secs (get-schema-value ?schema stop-secs))
                  (if (> ?stop-secs ?current-secs) then
                     (if (< ?wait ?time) then
                        (replace-with-shorter-interval ?schema ?action)))
                  (if (<= ?stop-secs ?current-secs) then
                     (if (eq ?status ?*pending-status*) then
                        (choose-agent-now ?name))
                     (if (eq ?status ?*proposed-status*) then
                        (process-intervention-agent-delete ?schema ?action))))
         (if (eq ?done no) then
            (if (eq ?wait 0) then
               (choose-agent-now ?name)
             else
               (load-proposed-intervention-pending ?action ?wait ?wait-unit ?current-secs))))
```

Pattern Formation and Condition Matching

- Several rules are used within the INTERPRET phase to control the formation of the physiologic patterns and matching of their conditions once a new set of data has been read.
- Each type of data, such as the hemodynamics, laboratory data, blood gases, etc. would have four such rules responsible for this particular task.
- Using a newly loaded set of hemodynamic data as an example, the first step is to invoke the INTERPRET-Hemodynamics rule to compute the exponential-smoothing average and trend, and to assign a pattern-code to each parameter based on the targe ranges. This is shown below.

```
(defrule INTERPRET-Hemodynamics
        (schema phase-control  (phase interpret.reference.ranges))
        (schema file-control end-of-file ~yes)
=>
        (for ?slot in-slots-of current-hemodynamics do
           (if (and (not (slotp current-state ?slot))) then
              (bind ?value (get-schema-value current-hemodynamics ?slot))
              (bind ?item (nth$ (nth$ ?value 1) 1))
              (if (/= ?item NIL) then
                  (compute-exp-smooth-avg current-hemodynamics previous-hemodynamics ?slot)
                  (compute-linear-trend current-hemodynamics ?slot linear-tend-hemo)
                  (assign-range-hemo current-hemodynamics ?slot)
               else
                  (carryover-info current-hemodynamics previous-hemodynamics ?slot))))
```

- Once the individual pattern-code digits become available, the INTERPRET-Pattern-Hemodynamics rule combines them to form a five-digit hemodynamic abnormality-pattern by shifting and adding the digits of the selected parameters to form a pattern.
- This rule also checks for any discrepancy in the PAWP-PAPD values by ignoring the PAPD pattern-code digit if the two differ more than a predefined limit. The rule is shown below.

```
(defrule INTERPRET-Pattern-Hemodynamics
        (schema phase-control  (phase interpret.derive.pattern))
        (schema current-hemodynamics
                (ABPM (?abpm ? ? ?abpm-code $?))(CI (?ci ? ? ?ci-code $?))
                (CVP (?cvp ? ? ?cvp-code $?))(HR (?hr ? ? ?hr-code $?))
                (PAWP (?pawp ? ? ?pawp-code $?))(PAPD (?papd ? ? ?papd-code $?)))
=>
        (if (numberp ?pawp) then
           (retract-all-schema-values last-cardiac-output ignore-papd)
           (if (>= (- (abs ?pawp)(abs ?papd)) ?*papd-pawp-difference*) then
              (bind ?papd-code 0)(put-schema-value last-cardiac-output ignored-papd yes))
        else
           (if (not (slot-null last-cardiac-output ignore-papd)) then (bind ?papd-code 0))
        (bind ?pattern (derive-pattern ?hr-code ?abpm-code ?ci-code ?papd-code ?cvp-code))
        (modify-schema-value current-state abnormality-hemo ?pattern)))
```

- Since each pattern contains one or more proposed diagnostic tests and/or intervention strategies, the next step is to record these interventions and trigger them at the appropriate time interval for processing.
- The trigger is done by looping through all of the proposed test and intervention slots of the pattern and copying the slot values into the corresponding subphase slot of the phase-control schema using the INTERPRET-Condition-Hemodynamics rule shown below.
- This rule also updates the current-state to indicate the current conditions present.

```
(defrule INTERPRET-Condition-Hemodynamics
        (schema phase-control
                (phase interpret.derive.condition))
        (schema current-state
                (is-a state)
                (abnormality-hemo ?pattern))
        (schema ?abnormality
                (is-a abnormality)
                (abnormality-type hemo))
        (schema ?clinical-condition
                (is-a clinical-condition)
                (abnormality-hemo $? ?pattern)
                (condition ?condition)
                (severity ?severity))
=>
        (if (slot-null ?abnormality abnormality-hemo-trend) then
           (bind ?current-condition (build$ ?severity ?condition))
           (put-schema-value current-state condition ?current-condition)
           (setup-subphase ?abnormality)))
```

- The last step involves the updating of the patient-selections schema to put the conditions into an active list, and the creation of a new condition schema for each of the conditions matched from the pattern.
- These steps are done with the INTERPRET-Update-Condition-Hemodynamics rule shown below.

```
(defrule INTERPRET-Update-Condition-Hemodynamics
        (schema phase-control
                (phase interpret.update.condition)
                (interval-avg (?interval ?interval-unit))
                (elapsed-time ?elapsed))
        (schema current-state
                (is-a state)
                (abnormality-hemo ?pattern))
        (schema ?abnormality
                (is-a abnormality)
                (abnormality-hemo ?pattern)
                (abnormality-type hemo))
        (schema ?clinical-condition
                (is-a clinical-condition)
                (abnormality-hemo $? ?pattern)
                (condition ?condition)
                (severity ?severity))
        (schema time-control
                (hemodynamic-date-time (?current-date ?current-time))
                (hemodynamic-in-secs ?current-secs))
=>
        (bind ?active-condition (get-schema-value patient-selections active-condition))
        (bind ?condition (build$ ?severity ?condition))
        (bind ?end-date-time (build$ ?current-date ?current-time))
        (if (eq (length$ ?active-condition) 0) then
          (if (/= ?severity ?*normal*) then
            (bind ?condition-schema (write-condition ?abnormality ?clinical-condition
                         ?condition ?begin-secs ?current-secs hemo))
            (put-schema-value patient-selections active-condition ?condition-schema))
         else
          (bind ?update (check-for-same-condition ?clinical-condition))
        (if (eq ?update yes) then
          (bind ?new-schema (write-condition ?abnormality ?clinical-condition ?condition
                         ?begin-secs ?current-secs hemo)))
          (put-schema-value patient-selections active-condition ?condition-schema)))
```

Time and I-O Controls

- Since the patient's data always arrive at different time intervals, it is necessary to keep track of the exact date and time a particular set of information was obtained. The date and time stamps are stored in a schema called the time-control schema, which is shown below.

```
(defschema time-control
        (admit-date-time (13-MAY-91 1250))
        (admit-in-secs 642045)
        (assess-interval (15 minutes))
        (bleeding-lookup (1 hours))
        (bloodgases-date-time (13-MAY-91 1500))
        (bloodgases-in-secs 642275))
        (bloodgases-delay (30 minutes))
        (cardiac-output-interval (2 3 4 hours))
        (cardiac-output-on-admission (1 hours))
        (collected-bloodgases-date-time (13-MAY-91 1430))
        (collected-bloodgases-in-secs 642245)
        (collected-laboratory-date-time (13-MAY-91 1400))
        (collected-laboratory-in-secs 642215)
        (hemodynamic-date-time (13-MAY-91 1605))
        (hemodynamic-in-secs 642340)
        (input-date-time (13-MAY-91 1605))
        (input-in-secs 642340)
        (laboratory-date-time (13-MAY-91 1500))
        (laboratory-delay (60 minutes))
        (laboratory-in-secs 642275)
        (last-redefine-date-time)
        (last-redefine-in-secs)
        (look-back (1 hours))
        (output-date-time (13-MAY-91 1600))
        (output-in-secs 642335)
        (redefine-range (2 hours))
        (redefine-range-fraction 0.8)
        (total-agents-kept (4 hours))
        (total-conditions-kept (1 hours))
        (total-critiques-kept (1 hours))
        (total-interventions-kept (2 hours))
        (total-hemodynamics-kept (2 hours))
        (wean-agent-range (2 hours))
        (wean-not-advised-between (2300 0500)))
```

- The date and time of the most recent set of hemodynamic data read is always assumed to represent the current date and time; any data set with a future date and time stamp is held and not processed until the current date and time have reached that future time point.
- All the date and time values are also stored internally as the total seconds elapsed since January 1, 1970 for computation purposes.
- An assumption was made that all laboratory results were available one hour after collection. A similar assumption was made with the blood gases that they would be available 30 minutes after collection. In both situations, since only the actual collection times were recorded in the case, one-hour or half-hour is added to the collection time. These are stored in different time slots within the time-control schema.
- Time intervals are also used to set the limits for retaining certain types of schemas such as any old interventions, critiques, conditions, and historical patient data, which are currently set to one or two hours. At the end of every cycle, a set of housekeeping rules would look up these time intervals and delete any old schemas that have past the predefined time limits.
- The assess-interval specifies when to assess the drug-dose effects; the look-back interval to indicate how far back to check if a recommendation has been made previously.
- The redefine-range and redefine-range-fraction are used as the criteria for redefining hemodynamic parameter range values.
- The wean-agent-range is used as the criteria for weaning therapeutic agents; the wean-not-advised-between time interval is when weaning should not be attempted (currently not used).

Two schemas have been created to handle the processing of the input and output:

- The first is the file-control schema that keeps track of the names and locations of the input data files, the status of the files as to whether they are open or closed, and whether there are any more input data for further reasoning.
- The second is the print-control schema that indicates the type of output to be produced, which is defined at run-time.
- Although the two schemas resemble more of the traditional data processing IO functions, they are important in ensuring the proper handling of the input data and the user interface for displaying the output, and are considered an integral part of the reasoning control knowledge.

Maintaining Patient States Over Time

- Every time a new set of patient data is read, it becomes part of the current state, with the old data set retained in the previous state for comparison. In addition, the previous data set would be stripped down with only the elapsed-time (in minutes) and its value stored as a sequence in the corresponding history schema.

- The maintenance is done at the PREPARE phase of the reasoning control via a number of house-keeping rules, and is also the last stage before the next processing cycle.
- For instance, when a new set of hemodynamic data is read, the old set is always moved to the previous-hemodynamics schema. The elapsed time and the hemodynamic value pair for each parameter are stripped and stored as a sequence in the history-hemodynamics schema. The latter schema is used to compute the hemodynamic trend. The same is done for the laboratory, blood gas and intake-output data.
- Several ARTIM functions have been developed to allow selected data to be retrieved from the previous and history schemas, such as the HCT or HB level within the last 12 hours. An example of the rules to update the previous and history schemas for the hemodynamic data is shown below.

```
(defrule PREPARE-Next-Hemodynamics
          (schema phase-control
                    (phase prepare.next.input)
                    (interval (?interval ?interval-unit))
          (schema current-state (elapsed-time ?elapsed))
          (schema file-control (read-hemo yes))
          (schema time-control
                    (hemodynamic-date-time ?date-time)
                    (hemodynamic-in-secs ?secs)
                    (total-hemodynamics-kept (?kept ?kept-unit))
=>        (if (schemap previous-hemodynamics) then
             (schemad previous-hemodynamics))
          (copy-schema current-hemodynamics previous-hemodynamics)
          (modify-schema-value previous-hemodynamics is-a previous-state)
          (for ?slot in-slots-of current-hemodynamics do
             (retract-all-schema-values current-hemodynamics ?slot))
          (if (not (schemap history-hemodynamics)) then
             (copy-schema patient-hemodynamics history-hemodynamics))
          (bind ?kept (convert-interval-to sec ?interval ?interval-unit))
          (bind ?skip (- ?elapsed ?kept))
          (for ?slot in-slot-of previous-hemodynamics do
             (if (not (slotp previous-state ?slot)) then
                (if (not (slot-null previous-hemodynamics ?slot)) then
                    (for ?seq in-slot-values-of previous-hemodynamics ?slot do
                       (bind ?result (strip-current-state ?seq)))
                   (put-schema-value history-hemodynamics ?slot ?result)
                    (if (> ?skip 0) then
                       (bind ?seq (get-schema-value history-hemodynamics ?slot))
                       (retract-all-schema-values history-hemodynamics ?slot)
                       (for ?sub-seq in$ ?seq do
                          (bind ?time (nth$ ?sub-seq 1))
                          (if (> ?time ?skip) then
                              (put-schema-value history-hemodynamics ?slot ?sub-seq))))))
```

THE END